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APPLERA CORP. AND TROPIX, INC.,
Petitioners,

v.

ENZO BIOCHEM, INC., ENZO LIFE SCIENCES, INC., AND YALE UNIVERSITY,
Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

PETITION FOR A WRIT OF CERTIORARI

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QUESTION PRESENTED

For a patent to be valid, its claims must be "definite"—the patent must include "claims *particularly pointing out* and *distinctly claiming* the subject matter which the applicant regards as his invention." 35 U.S.C. § 112 ¶ 2 (emphasis added). The Federal Circuit holds that this requirement of "particular[ity]" and "distinct[ness]" is satisfied so long as claim language is not "insolubly ambiguous," or is merely capable of being construed. The question presented is:

Whether the Federal Circuit's standard for definiteness is consistent with the language of § 112.

PARTIES TO THE PROCEEDING

All parties to the proceeding are identified in the caption.

RULE 29.6 STATEMENT

Petitioner Applera Corporation was formerly made up of two business units, Applied Biosystems and Celera Genomics. In 2008 Applied Biosystems merged with a subsidiary of Invitrogen Corporation to form Applied Biosystems, LLC. Celera Genomics has been split off into an independent company, Celera Corporation.

Invitrogen Corporation is now known as Life Technologies Corporation, and wholly owns Applied Biosystems, LLC. Celera Corporation and Life Technologies Corporation are both publicly traded. No publicly held company owns more than 10% of either Celera Corporation's or Life Technologies Corporation's stock.

Tropix, Incorporated was purchased by Applera Corporation and no longer exists as a separate legal entity.

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PETITION FOR A WRIT OF CERTIORARI

Applera Corporation and Tropix, Incorporated (collectively, "Applera") respectfully petition for a writ of certiorari to review the judgment of the United States Court of Appeals for the Federal Circuit.

OPINIONS BELOW

The opinion of the United States District Court for the District of Connecticut, which granted summary judgment to Applera that the patent claims asserted by Respondents are invalid, is available at 2007 WL 2669025, and is reproduced in the appendix to this petition (Pet. App.) at 34a-73a. The opinion of the Federal Circuit is reported at 599 F.3d 1325, and reproduced at Pet. App. 1a-33a. The Federal Circuit's order denying panel rehearing and rehearing en banc, accompanied by Judge Plager's opinion dissenting from the denial of panel rehearing, is reported at 605 F.3d 1347, and reproduced at Pet. App. 74a-79a.

JURISDICTION

The court of appeals entered judgment on March 26, 2010. Pet. App. 1a. A timely petition for rehearing and rehearing en banc was denied on May 26, 2010. Pet. App. 74a-75a. The jurisdiction of the court of appeals was based on 28 U.S.C. § 1295(a)(1). On August 11, 2010, Chief Justice Roberts granted an extension of time to and including September 23, 2010, to file a petition for a writ of certiorari. This Court has jurisdiction pursuant to 28 U.S.C. § 1254(1).

STATUTORY PROVISION INVOLVED

The federal Patent Act provides in relevant part as follows:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. § 112 ¶ 2.

INTRODUCTION

The statutory requirement of definiteness—that a patent's claims "*particularly* point[] out and *distinctly* claim[] the subject matter which the applicant regards as his invention," 35 U.S.C. § 112 ¶ 2[1]—is of surpassing importance. It is a basic requirement that must be satisfied for a patent to be issued or enforced, and so it affects every pending U.S. patent application, every issued U.S. patent, and many if not all U.S. federal-court patent cases. This requirement also is central to the proper functioning of the patent system. At the heart of that system is a basic bargain: Inventors are granted a limited monopoly in exchange for making their invention public. For this system to operate fairly and effectively, the inventor must provide clear notice to the public of the invention's metes and bounds, or else the patent system will discourage rather than encourage invention:

> "[T]he limits of a patent must be known for the protection of the patentee, the encouragement of the inventive genius of others and the assurance that the subject of the patent will be dedicated ultimately to the public." Otherwise, a "zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims would discourage invention only a little less than unequivocal foreclosure of the field,"

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[1] Emphases are added throughout this petition unless otherwise noted.

> and "[t]he public [would] be deprived of rights supposed to belong to it, without being clearly told what it is that limits these rights."

Markman v. *Westview Instrs., Inc.*, 517 U.S. 370, 390 (1996) (alterations in original) (quoting *General Electric Co.* v. *Wabash Appliance Corp.*, 304 U.S. 364, 369 (1938); *United Carbon Co.* v. *Binney & Smith Co.*, 317 U.S. 228, 236 (1942); and *Merrill* v. *Yeomans*, 94 U.S. 568, 573, (1877)).

Since this Court last addressed the fundamental requirement of definiteness more than half a century ago, the Federal Circuit has departed radically from the statute's language, in derogation of the patent system's basic purpose. In this and a series of other cases, that court has created precisely the "zone of uncertainty" that this Court declared antithetical to innovation. In the decision below, the Federal Circuit concluded that a patent is definite where it provides "at least some guidance" about the boundaries of its claims. Pet. App. 14a. This toothless standard is emblematic of the Federal Circuit's basic approach, articulated in this case and elsewhere, that a claim is definite if it is merely "capable of being construed" or, put otherwise, not "insolubly ambiguous." In short, here as elsewhere, the Federal Circuit has adopted a rule that departs from the statutory language and does serious violence to the statutory purpose. Cf. *KSR Int'l Co.* v. *Teleflex, Inc.*, 550 U.S. 398, 415-18 (2007) (rejecting the Federal Circuit's "TSM" test for obviousness); *Bilski* v. *Kappos*, 130 S. Ct. 3218, 3225-26 (2010) (rejecting "machine-or-transformation" test as the sole test for determining the patentability of business methods).

This Court's review also is warranted because the Federal Circuit's test for indefiniteness conflicts with the more rigorous standard adopted by the Patent

and Trademark Office (PTO). The PTO has flatly rejected the Federal Circuit's "insolubly ambiguous" standard, and employs a more demanding standard for definiteness—i.e., it uses "a lower threshold of ambiguity when reviewing a pending claim for indefiniteness than those used by [the Federal Circuit]." *Ex parte Miyazaki*, No. 2007-3300, 2008 WL 5105055, at *5 (B.P.A.I. Nov. 19, 2008). This conflict is unsustainable. "One of the fundamental purposes behind the Patent and Copyright Clauses of the Constitution was to promote national uniformity in the realm of intellectual property." *Bonito Boats, Inc.* v. *Thunder Craft Boats, Inc.*, 489 U.S. 141, 162 (1989); accord *Markman*, 517 U.S. at 390 (noting "the importance of uniformity in the treatment of a given patent"). This Court should grant certiorari to resolve this conflict between the federal agency that has responsibility for granting and issuing patents, see 35 U.S.C. § 2, and the federal appeals court that has exclusive appellate jurisdiction over patent litigation, see 28 U.S.C. § 1295(a). In the alternative and at a minimum, this Court should call for the views of the Solicitor General, as it has done in other recent cases presenting important questions arising under the Patent Act.

STATEMENT OF THE CASE

I. STATUTORY BACKGROUND

"The Congress shall have power ... [t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." U.S. Const. art. I, § 8, cl. 8. Congress has effectuated this constitutional imperative by granting to inventors limited exclusivity in exchange for "precision of disclosure" of what they have invented. *Universal Oil Prods. Co.* v. *Globe Oil & Ref. Co.*, 322 U.S. 471, 484

(1944) ("[T]he *quid pro quo* [for the patent right] is disclosure of a process or device in sufficient detail to enable one skilled in the art to practice the invention once the period of the monopoly has expired, and the same precision of disclosure is likewise essential to warn the industry concerned of the precise scope of the monopoly asserted.").

In establishing the patent system, Congress enacted statutory requirements dictating how patents must be structured and limiting what they may cover. 35 U.S.C. § 112 requires each patent to include a "specification." The specification must "contain a written description of the invention, and the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art ... to make and use" the invention. 35 U.S.C. § 112 ¶ 1. Section 112 further requires that the specification "conclude with one or more claims *particularly pointing out* and *distinctly claiming* the subject matter which the applicant regards as his invention." *Id.* ¶ 2. If a patent is granted, it is these "claims" (rather than the specification, for instance) that set the boundaries of the patent right. *Markman*, 517 U.S. at 373; see also *Fuji Photo Film Co.* v. *ITC*, 386 F.3d 1095, 1106 (Fed. Cir. 2004) ("[i]t is a familiar axiom of patent law" that limitations in the specification are not to be imported into the claims).[2]

A single patent may contain multiple claims, and indeed this is common practice. Each claim may form

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[2] The first step in patent litigation is typically "claim construction," the process of interpreting the language used in the claims. *See, e.g.*, *Phillips* v. *AWH Corp.*, 415 F.3d 1303, 1312-19 (Fed. Cir. 2005) (en banc). In construing claim language, the reviewing court attempts to determine how a person of ordinary skill in the art would understand the terms. *Id.* at 1313.

the basis for a claim of infringement. Here, for instance, one of the three patents at issue contained 71 separate claims. Federal Circuit Joint Appendix ("CAFC JA") 182-85. Some of those claims were "independent"—i.e., they were freestanding and did not refer to any other claims in the patent. Others were "dependent"—they incorporated the limitations set forth in a previous claim in the patent, and added some further limitation. See 35 U.S.C. § 112 ¶¶ 3-4.

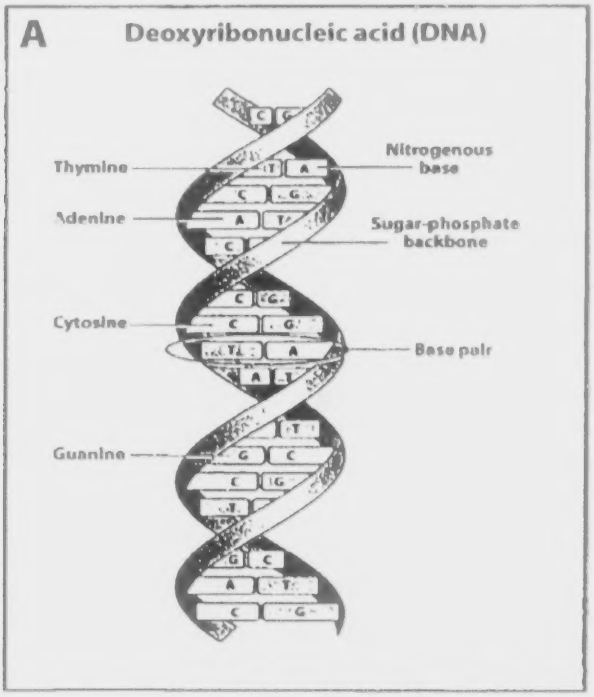
Separate from whether a patent has been infringed-- a question that is not at issue in this appeal—is whether a patent claim is "valid." The Patent Act establishes various bases upon which a claim may be invalid, and these operate as defenses to a claim of infringement. If, for instance, a claim is so broad that it covers what already has been done or disclosed, it is invalid for lack of novelty. See *id.* § 102. If a claim merely covers obvious modifications to what previously has been done or disclosed, then a patent is invalid for "obviousness." *Id.* § 103; see *KSR*, 550 U.S. at 417-18. If the patent specification does not provide a description that would permit one of ordinary skill in the art to implement the full scope of what is claimed without undue experimentation, the claim is invalid for lack of enablement. See, *e.g.*, *ALZA Corp.* v. *Andrx Pharms., LLC*, 603 F.3d 935, 940 (Fed. Cir. 2010).

And, pertinent here, if the claim does not "particularly point[] out and distinctly claim[]" the invention, then it is invalid as "indefinite." 35 U.S.C. § 112 ¶ 2. Definiteness serves a critical notice function: A claim must "inform the public during the life of the patent of the limits of the monopoly asserted, so that it may be known which features may be safely used or manufactured without a license and which may not." *Permutit Co.* v. *Graver Corp.*, 284 U.S. 52, 60 (1931).

This "statutory requirement of particularity and distinctness in claims is met only when they clearly distinguish what is claimed from what went before in the art and clearly circumscribe what is foreclosed from future enterprise." *United Carbon*, 317 U.S. at 236.

II. THE TECHNOLOGY AT ISSUE

This litigation involves a dispute over patents concerning technology for detecting nucleic acids such as DNA and RNA. See Pet. App. 2a, 4a-5a. DNA and RNA store in coded form the genetic information in human cells. See generally *In re O'Farrell*, 853 F.2d 894, 896-98 (Fed. Cir. 1988). They are composed of nucleotides that are linked together to form "polynucleotide" chains. This diagram shows two such chains joined together in the famous "double helix":



CAFC JA 7527.[3]

Important to the structure of the nucleotides—and to the diagnostic technology at issue here—are nitrogenous bases. These bases form the rungs in the ladder-shaped structure shown above. DNA and RNA generally contain four types of bases: cytosine (C), thymine (T), adenine (A), and guanine (G). Pet. App. 2a.[4] Each rung is composed of two bases, and the bases organize themselves in a predictable fashion—C goes with G, and A goes with T. As a result, one polynucleotide chain will pair, or "hybridize," with a complementary chain composed of complementary bases. *Id.* at 3a. If, for instance, one had a chain AATTCCGG, its complementary chain would be TTAAGGCC. As with the order of letters in this sentence, it is the order of bases in DNA that convey information. This information is called the DNA's "sequence." Due to the predictable fashion in which DNA strands pair, the sequence of one DNA chain can be derived from its complementary chain, like a photographic print from a negative.

It is often desirable to determine whether a test sample contains a particular DNA sequence—for instance, to identify the presence of a gene that predicts a higher risk of a certain cancer. This can be done by creating a "probe" composed of a sequence of nucleotides, which will hybridize with the test sample if a complementary nucleotide sequence is present. To assist in determining whether such hybridizing has occurred, a detectable "label" is attached to the probe.

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[3] RNA generally exists in a single-stranded form. Like DNA, however, a single strand of RNA can pair with a complementary strand. CAFC JA 7526.

[4] In RNA, uracil replaces thymine as the complementary base to adenine. Pet. App. 2a-3a.

The probe is introduced into the test sample; hybridizing (if any) occurs; any unhybridized material is removed; and, if the probe hybridized with the test sample, the label should be detectable in the sample. This process is illustrated in the diagram reproduced at Pet. App. 81a.

The patents at issue here concern nucleotide labels. Pet. App. 4a-5a.[5] The patents (which share a common specification) explain that the label can be attached directly to a probe via the nitrogenous base of a nucleotide. The label also can be attached to the probe through an intermediate "linkage group." It is this limitation of the patent concerning linkage groups that gives rise to the indefiniteness issue in this case. *Id.* at 4a-5a, 10a-11a. The patent claims at issue do not specify any particular linkage group or groups to use. Rather, the linkage group can be any chemical structure that does not "'interfer[e] substantially'" with the detection probe's function. *Id.* at 4a-5a.[6] The patent also does not define how much interference is "substantial."

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[5] *See* U.S. Patent Nos. 5,476,928, 5,449,767, and 5,328,824. Specifically, the claims of the three patents are directed to a nucleotide compound, modified with a detectable label, that can be used as a detection probe; or to a method of using such a nucleotide compound as a detection probe.

[6] Specifically, these patents claim a linkage group that does "not interfer[e] substantially with the characteristic ability of said compound to hybridize with said nucleic acid or of A to be detected" ('824 patent col. 31, ll. 31-34); "does not substantially interfere with the characteristic ability of the oligo- or polynucleotide to hybridize with a nucleic acid and does not substantially interfere with formation of the signaling moiety or detection of the detectable signal" ('767 patent col. 31, ll. 2-7); and does "not interfere[e] substantially with detection of A." ('928 patent col. 30, ll. 29-30).

III. PROCEEDINGS BELOW

A. In a complaint filed in the United States District Court for the District of Connecticut, Enzo Biochem, Inc., Enzo Life Sciences, Inc., and Yale University (collectively "Enzo") sued Applera for patent infringement. On October 12, 2006, the district court construed the patents' disputed claim terms. CAFC JA 32-66. Among other things, the district court construed the functional claim limitations "not interfering substantially with" and "does not substantially interfere."[7] *Id.* at 42-44. Adopting Enzo's proposed construction, the court determined that this functionality applied to both hybridization and detection; under the construction, "'the linkage group neither substantially interferes with the ability of the compound to hybridize with the nucleic acid nor substantially interferes with the ability of A to be detected.'"[8] Pet. App. 52a; see also CAFC JA 44.

The district court granted summary judgment to Applera, holding that the asserted claims are invalid because they are indefinite. The court's ruling focused on the "substantially interfere" limitation, concluding that the "specifications neither set forth how one would gauge substantial interference, nor delimit

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[7] A "functional claim limitation" defines something by what it does or does not do, "rather than by what it is." U.S. Dep't of Commerce, *Manual of Patent Examining Procedure* 2173.05(g) (8th ed. rev. 2010).

These terms appear in claims 1, 42, and 48 of the '767 patent, CAFC JA 182-85; claim 1 of the '824 patent, *id.* at 161-62, and claims 1 and 2 of the '928 patent, *id.* at 202-03.

[8] Although the Federal Circuit *sua sponte* modified the district court's construction as to one of the three patents, *see* Pet. App. 13a, the modification did not alter the construction of "not interfering substantially," and the construction of that critical phrase was not challenged on appeal.

the threshold at which interference with the procedure prevents [the claimed] method from being implemented." Pet. App. 60a. The court explained that

> substantial interference has thus been left to the experimenter to determine the conditions under which detection and hybridization either succeeds or fails. Although the patent expresses a term of degree ("substantial interference"), expert testimony has shown the term to be an illusory yardstick which, if permitted to stand, would sweep all successful hybridization and detection into the ambit of the patents' coverage, while excluding any unsuccessful procedures ....

Id.

The district court independently granted summary judgment to Applera on the ground that the asserted claims of the '767, '824 and '928 patents were invalid under 35 U.S.C. § 102 as anticipated by prior art. Pet. App. 61a-73a.

B. The Federal Circuit reversed, concluding that the asserted claims were sufficiently definite. It reiterated its established standard that "[i]f a claim is indefinite, the claim, by definition, cannot be construed." Pet. App. 10a (citing *Honeywell Int'l, Inc.* v. *ITC*, 341 F.3d 1332, 1342 (Fed. Cir. 2003)). The court found it significant that although the claims do not define "substantially," nor specify how to measure what amount of interference would be "substantial," "[t]he claims in this case provide *at least some guidance* as to how much interference will be tolerated." *Id.* at 14a.

The court found "some guidance" in various "examples" of linkage groups identified in the patents. For instance, in each patent, one dependent claim (not asserted in this litigation as a basis for infringement)

showed a linkage group with a particular structure. Pet. App. 14a-15a. The court reasoned that one could "presume that" this structure "will perform [the] function required of that structure" in the asserted, independent claim. *Id.* at 14a. The court did not address or conclude whether the use of this structure established the boundaries of the claim, nor did the court of appeals modify the claim construction to do so.

Next, and to similar effect, the court noted that "[t]he specification provides additional examples of suitable linkage groups, including some criteria for selecting them." Pet. App. 15a. The court did not conclude that these "examples" establish either a floor or ceiling for measuring how much interference is "substantial." This also was true of the "criteria for selecting" linkage groups. The first criterion was simply that a linkage group could "'withstand all experimental conditions to which normal nucleotides and polynucleotides are routinely subjected.'" *Id.* Second, the court noted the specification's reference to experiments in which melting temperature was used as a proxy for interference. *Id.* at 15a-16a. Two experiments using different probes were reported as producing acceptable results. Neither was identified as establishing an outer boundary of what constitutes substantial interference. *Id.*

Finally, the court cited to the patents' prosecution history to identify eight examples of "specific linkage groups that ... did not substantially interfere with hybridization or detection." Pet. App. 16a. The court did not address, much less decide, whether these linkage groups establish the outer boundaries of the claimed invention.

As noted above, the claims preclude substantial interference with both "hybridization" and "detection."

Turning to detection, the court held the "substantial interference" limitation not indefinite for "most of the same reasons discussed in connection with 'hybridization.'" Pet. App. 18a. The court again cited the eight examples of linkage groups described in the prosecution history. It reasoned that, if testing a potentially infringing product revealed detection "using the exemplary linkage groups," then "a person of ordinary skill would understand that a different linkage group ... likewise does not 'substantially interfere' with ... detection." *Id.* at 19a.

C. The Federal Circuit denied Applera's petition for panel rehearing and rehearing en banc. Pet. App. 75a. Judge Plager dissented, and would have granted panel rehearing. *Id.* at 75a-79a. He began by harshly criticizing the law of indefiniteness as it has developed in the Federal Circuit:

> Despite the varying formulations that this court has used over the years in describing its 'indefiniteness' jurisprudence ..., the general conclusion from our law seems to be this: if a person of ordinary skill in the art can come up with a plausible meaning for a disputed claim term in a patent, that term, and therefore the claim, is not indefinite.

Id. at 75a. The result is the evisceration of the notice function at the heart of the patent system:

> The corollary derived from this understanding is that if several persons of ordinary skill come up with competing but plausible interpretations of a disputed term—as is typically the case with competing "expert witnesses" in patent infringement litigation—the problem is not one of an inherently ambiguous and potentially indefinite claim term, but rather the problem becomes

> simply one of picking the "right" interpretation for that term. Since picking the "right" interpretation—claim construction—is a matter of law over which this court rules, and since the view of the trial judge hearing the case is given little weight, so that the trial judge's view on appeal becomes just a part of the cacophony before this court, it is not until three court of appeals judges randomly selected for that purpose pick the "right" interpretation that the public, not to mention the patentee and its competitors, know what the patent actually claims.

Id. at 76a-77a (footnote omitted).

In contrast to the approach adopted by the Federal Circuit, Judge Plager explained, the PTO is "taking steps to give the statutory requirement real meaning." Pet. App. 77a. He quoted a "rare precedential opinion" of the Board of Patent Appeals (BPAI), which expressly rejected the Federal Circuit's interpretation of the statute. *Id.* at 77a-78a. The BPAI has held that in reviewing patent applications, "'if a claim is amenable to two or more plausible claim constructions, the USPTO is justified in requiring the applicant to more precisely define the metes and bounds of the claimed invention by holding the claim unpatentable under 35 U.S.C. § 112, second paragraph, as indefinite.'" *Id.* at 78a (quoting *Ex parte Miyazaki*, 2008 WL 5105055, at *5).

Judge Plager went on to explain that, "if the public notice function of the patent law is to be honored, claim terms must particularly point out and distinctly claim the subject matter of the invention. In my view, this court's definiteness doctrine could go considerably further in promoting that objective than it currently does, with the not inconsequential benefit of shifting the focus from litigation over claim con-

struction to clarity in claim drafting." Pet. App. 78a-79a. Simply and starkly put: "It is time for us to move beyond sticking our fingers in the neverending leaks in the dike that supposedly defines and figuratively surrounds a claimed invention. Instead, we might spend some time figuring out how to support the PTO in requiring that the walls surrounding the claimed invention be made of something other than quicksand." *Id.* at 79a.

REASONS FOR GRANTING THE PETITION

The Federal Circuit's decisions interpreting the statutory requirement of definiteness have departed from the statutory text and are inconsistent with this Court's precedent. As this Court has explained, the definiteness requirement serves the essential function of ensuring that the public will have clear notice of the boundaries of a claimed invention. Only when there is such clarity can the public determine with confidence what area is reserved to the patentee.

The Federal Circuit's test does not satisfy the statute's purpose. According to that court, a claim is indefinite only if it cannot be construed at all or is "insolubly ambiguous." The scope of a monopoly should not be measured with so indeterminate a yardstick. The statute requires affirmative certainty about the scope of a claim, but the Federal Circuit in stark contrast requires only a slight lack of uncertainty—or, as the Federal Circuit put it here, "some guidance" as to what is off-limits.

By contrast, the PTO applies a more rigorous interpretation of the statute, rejecting a claim as indefinite if it is subject to two or more plausible constructions. The agency has expressly declined to follow the Federal Circuit's interpretation of the statute. This Court's review is warranted to resolve this funda-

mental conflict, and to correct the Federal Circuit's departure from the text of the Patent Act.

I. THE FEDERAL CIRCUIT HAS DEPARTED FROM THE TEXT OF § 112 AND THIS COURT'S PRECEDENTS CONSTRUING IT.

A. The Statutory Language Requires That Patent Claims Be Defined With Particularity And Distinctness.

It is a fundamental requirement of federal patent law that "[t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112 ¶ 2. This Court has emphasized for more than a century that a patent claim must state with specificity the boundaries of the domain that it would seek to monopolize. "The claim is a statutory requirement, prescribed for the very purpose of making the patentee define precisely what his invention is ...." *White* v. *Dunbar*, 119 U.S. 47, 52 (1886). Accordingly, "[t]he statutory requirement of particularity and distinctness in claims is met only when they clearly distinguish what is claimed from what went before in the art and clearly circumscribe what is foreclosed from future enterprise." *United Carbon*, 317 U.S. at 236; accord *General Electric*, 304 U.S. at 369 ("claimed inventions, improvements and discoveries ... require *precise descriptions* of the new characteristic for which protection is sought"); see also *The Incandescent Lamp Patent*, 159 U.S. 465, 475 (1895) (a patent "'should state the component parts of the new manufacture claimed *with clearness and precision*'"); *Merrill*, 94 U.S. at 573 ("[T]he patent law ... leave[s] no excuse for ambiguous language or vague descriptions.").

This specificity serves multiple essential goals. It is necessary to "inform the public during the life of the patent of the limits of the monopoly asserted, so that it may be known which features may be safely used or manufactured without a license and which may not." *Permutit*, 284 U.S. at 60. This is because "[t]he [patent] monopoly is a property right; and like any property right, its boundaries should be clear. This clarity is essential to promote progress, because it enables efficient investment in innovation. A patent holder should know what he owns, and the public should know what he does not." *Festo Corp.* v. *Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 730-31 (2002); see also *Merrill*, 94 U.S. at 573 ("The public should not be deprived of rights supposed to belong to it, without being clearly told what it is that limits these rights.").

Conversely, allowing uncertain claim language undermines the patent system's fundamental goal of encouraging innovation: "A zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims would discourage invention only a little less than unequivocal foreclosure of the field." *United Carbon*, 317 U.S. at 236. Such uncertainty therefore confers an unreasonable benefit on patent owners, at the expense of the public:

> The limits of a patent must be known for the protection of the patentee, the encouragement of the inventive genius of others and the assurance that the subject of the patent will be dedicated ultimately to the public. The statute seeks to guard against unreasonable advantages to the patentee and disadvantages to others arising from uncertainty as to their rights.

General Electric, 304 U.S. at 369 (footnote omitted). In addition, clarity in claim-drafting "enable[s] courts

to determine whether novelty and invention are genuine." *United Carbon*, 317 U.S. at 236. The looseness of the Federal Circuit's standard over the years has encouraged patent draftsmen to be less rather than more clear, as this uncertainty itself confers substantial benefits to the patentholder—it keeps competition away, and makes infringement litigation more expensive for those intrepid enough to test the limits of an existing patent.

B. The Federal Circuit Requires Only That Patent Claims Not Lack Total Ambiguity.

1. The Federal Circuit has created a separate test that is unfaithful to these core principles. A claim is statutorily "definite," the Federal Circuit repeatedly has held, if it is "capable of" or "amenable to construction." *E.g.*, *Source Search Techs. LLC* v. *LendingTree LLC*, 588 F.3d 1063, 1076 (Fed. Cir. 2009); *Ultimax Cement Mfg. Corp.* v. *CTS Cement Mfg. Corp.*, 587 F.3d 1339, 1352 (Fed. Cir. 2009); *Young* v. *Lumenis, Inc.*, 492 F.3d 1336, 1346 (Fed. Cir. 2007); *Honeywell*, 341 F.3d at 1338; *Exxon Research & Eng'g Co.* v. *United States*, 265 F.3d 1371, 1376-80 (Fed. Cir. 2001); see Pet. App. 10a (claim is indefinite if it "cannot be construed"). This rule is erroneous for multiple reasons, and this Court should grant review to bring the Federal Circuit into conformity with the statute and this Court's decisions.

As an initial matter, this standard disregards the reality of claim construction. The mere fact that a claim has been construed does not mean that it cannot be indefinite. During the process of claim construction, a district court does its utmost to interpret and give content to disputed claim terms. But not every claim term will thereby be clarified. And, where particular terms within a claim are unclear, a

court sometimes will construe them with a bare synonym, or not at all, sometimes leaving the question of definiteness for another day. In this case, for instance, the district court construed the claim terms using the phrase "not interfer[e] substantially" with a synonym: "neither substantially interferes." Pet. App. 52a; see also CAFC JA 44. It gave the term no further detail or content, and took this approach at the behest of Enzo, which itself recognized that indefiniteness could result: "If the defendants want to raise an issue with respect to validity at a later date, that's perfectly fine. In fact, the Court should faithfully interpret 'substantially interfering,' and if it's indefinite, then we'll have to live with that." CAFC JA 1644-47.

More fundamentally, the Federal Circuit's indefiniteness standard is by its terms radically different than the statutory requirement. Indeed, the two approaches are nearly opposite. Section 112 imposes an affirmative requirement of "particular[ity]" and "distinct[ness]," which this Court holds requires "clear[]" distinctions," and "precis[ion]." *Supra* at 16-18. Under the Federal Circuit's "capable of construction" jurisprudence, however, a claim is definite so long as it is merely not "insolubly ambiguous." See, *e.g.*, *Honeywell Int'l Inc.* v. *United States*, 609 F.3d 1292, 1301-02 (Fed. Cir. 2010); *Power-One, Inc.* v. *Artesyn Techs., Inc.*, 599 F.3d 1343, 1348 (Fed. Cir. 2010); *Ultimax*, 587 F.3d at 1352.

That lesser standard requires nothing like "particularity" or "precision." Under Federal Circuit law, claim terms "are insolubly ambiguous," and thus indefinite, "only if they provide *no guidance* to those skilled in the art as to the scope of" the invention. *Power-One*, 599 F.3d at 1348; compare Pet. App. 14a (holding the claims at issue here not indefinite be-

cause they "provide at least some guidance as to how much interference will be tolerated"). Thus, as Judge Plager explained, a claim will be held definite "if a person of ordinary skill in the art can come up with a plausible meaning for a disputed claim term." Pet. App. 75a (citing cases). In case after case, the Federal Circuit has held that definiteness requires only a bare modicum of detail. If a reviewing court can put together any construction of the claim terms, the Federal Circuit holds, they necessarily are not indefinite. *See Bd. of Regents* v. *BENQ Am. Corp.*, 533 F.3d 1362, 1368 n.4 (Fed. Cir. 2008) ("As we have been able to discern a construction for the term 'syllabic element,' we reject BENQ's argument that this term is indefinite."). A claim is indefinite only where an accused infringer is entirely unable to ascertain "'*any* reasonable meaning'" of the term. *Young*, 492 F.3d at 1346; *Ultimax*, 587 F.3d at 1352; *Datamize LLC* v. *Plumtree Software, Inc.*, 417 F.3d 1342, 1347 (Fed. Cir. 2005).

The Federal Circuit's test subverts the statutory notice function. If definiteness only requires some plausible construction, then there can be no notice, because the public will not be given reasonable certainty in advance of its rights. Indeed, the scope of such a patent claim is necessarily uncertain until litigation is finally completed, which is only after the parties' experts and even disagreeing Federal Circuit judges have had their say. Pet. App. 76a-77a (Plager, J., dissenting). But cf. *United Carbon*, 317 U.S. at 236 ("A zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims would discourage invention only a little less than unequivocal foreclosure of the field.").

In short, the Federal Circuit's bare-bones requirement is miles removed from the standard articulated

in the statute, and is distinctly at odds with this Court's emphasis that claim language must provide the public with certainty—not merely "some guidance"—about the scope of a patent in order to achieve the statute's essential notice function. See *General Electric*, 304 U.S. at 369 ("The statute seeks to guard against unreasonable advantages to the patentee and disadvantages to others arising from uncertainty as to their rights.").

2. That the basic notice function has passed by the wayside in the Federal Circuit is clear from a line of cases in which that court has held claims definite based on the existence of nothing more than mere examples of what the patent is meant to cover—regardless whether the examples permit one to determine the actual *boundaries* of the claim.

Thus, in *Exxon Research*, the court found a claim using the term "for a period sufficient" to be definite, even though the patent did not "quantify the 'period sufficient' limitation by reference to any specific period or range of periods." 265 F.3d at 1378. The claim was not indefinite, the court held, because one of skill in the art could look to an example of a "period sufficient" that was described in the patent's specification. *Id.* at 1378-79. It was enough that the public could see at least one use of the language that was within the scope of the claim. See also, *e.g.*, *Hearing Components, Inc.* v. *Shure Inc.*, 600 F.3d 1357, 1367 (Fed. Cir. 2010) (finding the claim term "readily installed and replaced by a user" to be not indefinite because "the written description gives a clear example of a wax guard that is 'readily installed and replaced by a user'"); *Kinetic Concepts, Inc.* v. *Blue Sky Med. Group, Inc.*, 554 F.3d 1010, 1022 (Fed. Cir.) (claim term "selected stage of healing" not indefinite because the patent's specification "provides several

examples of selected stages of healing"), *cert. denied*, 130 S. Ct. 624 (2009).

Here, the Federal Circuit's ruling on indefiniteness depended principally on such examples. *Supra* at 11-13; see Pet. App. 14a-16a. For instance, the court focused on "eight specific linkage groups that Enzo declared did not substantially interfere with hybridization or detection." Pet. App. 16a. But the functional language used in the claims encompasses an infinitely larger group of chemicals—which was made clear by the specification's identification of choices of bonds that might be included in the chemical structure—and these examples do not circumscribe the limits of what structures could be used.

Providing a few examples from a vast category of potential choices identified in a patent's specification does not satisfy the statutory notice function. They do not mark the boundaries of the claims, not least of all because such examples do not limit the scope of the claims. See, *e.g.*, *Fuji Photo Film*, 386 F.3d at 1106. Rather, examples in the specification are simply illustrative of the claimed invention. At most, they therefore serve to identify particular instances of products, methods or the like that would infringe if unlicensed. So while examples may provide "some guidance" as to the meaning of the claim terms, Pet. App. 14a, they do not demarcate the metes and bounds of the invention, nor the area that remains free for experimentation—much less do they define those boundaries with particularity, clarity or precision.[9]

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[9] As a corollary to its rule that a claim cannot be indefinite if it has been construed, the Federal Circuit holds (and reaffirmed here) that the defenses of indefiniteness and anticipation are mutually exclusive: "If a claim is indefinite, the claim, by defini-

II. THE FEDERAL CIRCUIT'S INTERPRETATION OF § 112 CONFLICTS WITH THE PTO'S.

As Judge Plager explained in his dissent, the PTO has expressly declined to follow the Federal Circuit's test. Rather than limiting indefiniteness to claims that are "insolubly ambiguous," the agency rejects any claim term that is subject to "two or more plausible constructions." As the Board of Patent Appeals and Interferences has explained:

> [W]e employ a lower threshold of ambiguity when reviewing a pending claim for indefiniteness than those used by [the Federal Circuit]. In particular, rather than requiring that the claims are insolubly ambiguous, we hold that if a claim is amenable to two or more plausible claim constructions, the USPTO is justified in requiring the applicant to more precisely define the metes and bounds of the claimed invention by holding the claim unpatentable under 35 U.S.C. § 112, second paragraph, as indefinite.

Ex parte Miyazaki, 2008 WL 5105055, at *5. This conflict alone merits this Court's review: The agency charged with issuing patents has expressly rejected the statutory test employed by the Federal Circuit, and the agency and the court are committed to these disparate standards. Because the Federal Circuit has exclusive jurisdiction over patent cases, a conflict with another regional court of appeals is unlikely, but

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tion, cannot be construed. Without a discernable claim construction, an anticipation analysis cannot be performed." Pet. App. 10a. This reasoning is flatly illogical. Even if the edges of a patent's claims are insufficiently precise to meet the statutory requirement of definiteness, the claim may be anticipated by prior art that falls clearly within the limits of those fuzzy outer boundaries.

this conflict between the Federal Circuit and the PTO is equally intolerable. Cf. *Keystone Bridge Co.* v. *Phoenix Iron Co.*, 95 U.S. 274, 278 (1877) ("the courts have no right to enlarge a patent beyond the scope of its claim as allowed by the Patent Office").

To be sure, the PTO has attempted to explain the divergence between these standards by suggesting that it may be appropriate to judge patent applications by a different standard than issued patents. *Ex parte Miyazaki*, 2008 WL 5105055, at *4-5. However, both the PTO and the Federal Circuit are interpreting and applying the same statutory language, which cannot and should not be subject to two different meanings. Neither patent applicants, nor those who might compete with them, should be put in the middle of the tug-of-war created by the PTO and the Federal Circuit's competing standards. Such disparate interpretations are inconsistent with the fundamental principle that statutes must be applied consistently in keeping with their plain text, see, *e.g.*, *Jimenez* v. *Quarterman*, 129 S. Ct. 681, 685 (2009), and with the constitutional goal of uniformity in patent law, *Bonito Boats*, 489 U.S. at 162. Notably, the PTO typically interprets other statutory invalidity doctrines in similar fashion to the Federal Circuit—including other doctrines arising under § 112.[10]

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[10] The PTO and the Federal Circuit employ the same tests for novelty, obviousness, written description and enablement, among others. *Compare, e.g.*, *Ariad Pharms., Inc.* v. *Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (affirming the "'fairly uniform standard'" for assessing the written description requirement of § 112 ¶ 1 articulated in earlier precedent), *and ALZA*, 603 F.3d at 943 (assessing enablement requirement of § 112 ¶ 1), *with Ex parte Kubin*, 83 U.S.P.Q.2d 1410, 1415-17 (B.P.A.I. 2007) (assessing enablement and written description requirements of § 112 ¶ 1), *aff'd*, 561 F.3d 1351 (Fed. Cir. 2009).

Even if there were some justification for the disparate standards on indefiniteness, it would be appropriate to call for the views of the Solicitor General. This is so not only because of the conflicting standards noted above, but also because the United States has questioned the Federal Circuit's interpretation of the definiteness requirement. In an amicus brief filed last year in a case being reheard en banc in the Federal Circuit, to which both the Department of Justice and the PTO Solicitor's Office were signatories, the United States noted that,

> although the statute demands that the claims "particularly point[] out and distinctly claim[] the subject matter which the inventor regards as his invention," the [Federal Circuit] has construed this requirement to require little more than that the claims not be "insolubly ambiguous." *Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001). *Cf. United Carbon v. Binney & Smith Co.*, 317 U.S. 228, 236 (1942) (interpreting same language under the 1870 Act to require that the claims "clearly distinguish what is claimed from what went before in the art and clearly circumscribe what is foreclosed from future enterprise").[11]

This interpretation of the statute, the United States wrote in a marked understatement, is "at a minimum, not compelled by the text of the Patent Act." U.S. Br. at 28.

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[11] Br. of the United States as Amicus Curiae on Rehearing En Banc in Support of Respondent at 28-29, *Ariad Pharm., Inc.* v. *Eli Lilly & Co.*, No. 2008-1248 (Fed. Cir. filed Nov. 19, 2009), *available at* http://patentdocs.typepad.com/files/amicus-brief---usa.pdf (hereinafter "U.S. Br.") (first two alterations in original).

This Court should grant the petition in order to resolve this conflict, or at a minimum it should ask the Solicitor General to provide the views of the United States on this important question of federal law, which is central to virtually every patent that is issued by the PTO or reviewed by the Federal Circuit.

III. THE DECISION BELOW IS A GOOD VEHICLE FOR RESOLVING THESE ISSUES.

The Federal Circuit's decision in this case vividly illustrates just how far the Federal Circuit has departed from the statutory language and the notice considerations underlying it. The decision below articulates and depends upon the test that is at the root of many of the problems in the Federal Circuit. Pet. App. 10a ("If a claim is indefinite, the claim, by definition, cannot be construed."). The decision below also illustrates more broadly the lax attitude toward indefiniteness that broadly prevails in the Federal Circuit. Far from focusing on the language of the statute or even core concerns of notice, the Federal Circuit stated here that the claims could be considered definite merely because they "provide at least *some guidance* as to how much interference will be tolerated." *Id.* at 14a. It is no accident that Judge Plager chose this case as the occasion to announce that the emperor has no clothes.

First, the decision below repeatedly relies on examples from the patent specification in support of its conclusion that the claims provide "some guidance." But these examples do not mark the boundaries of what is claimed. They are not used in the independent claims, and do not limit the patent's scope; the court of appeals cited, for instance, examples of linkage groups identified in the specification and in the prosecution history. It even relied on examples that appear in dependent claims which are, by definition,

of narrower scope than the independent claims that were asserted in the litigation. *E.g.*, Pet. App. 14a ("A person of ordinary skill would presume that a structure recited in a dependent claim will perform a function required of that structure in an independent claim."); *supra* at 11-12 (describing dependent claims).

Highlighting the lack of meaningful guidance provided even by the narrower dependent claims, elsewhere in its opinion the Federal Circuit observed that there were an "infinite variety of linkage groups" having this "'more preferred'" structure, and even the linkage groups that it earlier had cited as providing "some guidance" would not necessarily perform the function required by the claims. Pet. App. 24a. In short, this case squarely presents the extraordinary situation in which the Federal Circuit has permitted data points to substitute for boundaries, contrary to the statutory requirement of particularity and distinctness.

Second, the patent claims that are at issue here contain functional claim limitations, which this Court has taken up more than once in evaluating definiteness.[12] As here, such claims are susceptible to being drafted very broadly, and the resulting uncertainty about the claims' scope means that a potential infringer would have to undertake "elaborate experimentation" after already having infringed in order even to determine whether it had infringed. *Holland*

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[12] *E.g.*, *Holland Furniture Co.* v. *Perkins Glue Co.*, 277 U.S. 245, 257 (1928) ("[o]ne attempting to use or avoid the use of Perkins' discovery as so claimed and described functionally could do so only after elaborate experimentation"); *see General Electric*, 304 U.S. at 371 ("the inventor ... uses conveniently functional language at the exact point of novelty"); *see also United Carbon*, 317 U.S. at 233-34 (considering functional claims).

Furniture Co. v. *Perkins Glue Co.*, 277 U.S. 245, 257 (1928).

This case well illustrates the problem. In order to "determine the exact level of detection achieved by the applicants using their exemplary linkage groups," Pet. App. 19a, could require millions of tests to evaluate every single molecule created using Applera's products. This is because, on the Federal Circuit's theory, whether a specific linkage group satisfies the "substantial interference" limitation depends on the "binding strength" of the DNA strand to which it is attached. *Id.* at 18a. That, in turn, will "depend on the length and sequence of the strand." *Id.* Because any change on the molecular level in the length or sequence of a strand could impact the degree of interference (and therefore infringement), the Federal Circuit's analysis means that the way to determine infringement is to test the binding strength of every DNA strand and compare it to the examples in the patent. Testing on this scale, by itself impractical if not impossible, is complicated still further by the fact that these molecules are created not by Applera but by its customers, typically in their own premises and long after they purchased the products. This regime is flatly incompatible with this Court's admonition that the statute requires claims to provide certainty about "the limits of the monopoly asserted, so that it may be known which features may be safely used or manufactured without a license and which may not." *Permutit*, 52 U.S. at 60.

Finally, this case illustrates how the laxity of the Federal Circuit's standard encourages patent owners to exploit the ambiguity surrounding the limits of their exclusive rights. Here, Enzo employed two technical experts who offered differing interpretations of what was required by the claim limitation in

question—a broad interpretation by one expert for infringement, and a narrower one by another for patent validity. One of the experts even conceded that under his interpretation, the claim terminology "'may mean different things to different people.'" See Pet. App. 57a (district court relying on this statement in holding the claims invalid). By adopting its atextual standard, the Federal Circuit has created an incentive for patent owners to adopt expansive or inconsistent interpretations of their patents, safe in the knowledge that the risk of a finding of indefiniteness is remote. This state of affairs epitomizes the "zone of uncertainty" against which this Court has warned.

In sum, this case paradigmatically illustrates the multiple problems that have infected the Federal Circuit's indefiniteness decisions. No other questions of fact or law risk hindering this Court's review of the Federal Circuit's indefiniteness ruling. The case is well-positioned for this Court's review.

CONCLUSION

For the foregoing reasons, this Court should grant the petition for a writ of certiorari.

Respectfully submitted,

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September 23, 2010

APPENDIX

APPENDIX A

UNITED STATES COURT OF APPEALS
FEDERAL CIRCUIT

No. 2009-1281

ENZO BIOCHEM, INC., ENZO LIFE SCIENCES, INC., AND YALE UNIVERSITY,
Plaintiffs-Appellants,

v.

APPLERA CORP. AND TROPIX, INC.,
Defendants-Appellees.

March 26, 2010

Before MICHEL, *Chief Judge*, PLAGER, and LINN, *Circuit Judges*.

LINN, *Circuit Judge*.

Enzo Biochem, Inc., Enzo Life Sciences, Inc., and Yale University (collectively, "Enzo") appeal the grant of summary judgment by the U.S. District Court for the District of Connecticut in favor of Applera Corp. and Tropix, Inc. (collectively, "Applera") that all asserted claims of U.S. Patents No. 5,328,824 ("the '824 patent"), No. 5,449,767 ("the '767 patent"), and No. 5,476,928 ("the '928 patent") are invalid as either indefinite or anticipated, and that U.S. Patent No. 5,082,830 ("the '830 patent") is not infringed. *Enzo Biochem, Inc. v. Applera Corp.*, No. 3:04-CV-929 (D.Conn. Mar. 5, 2009). Because we conclude that the

claims of the '824 and '767 patents are not indefinite, and because we find genuine issues of material fact as to anticipation, we reverse the district court's summary judgment of invalidity of those two patents. Although we find that the '928 patent is not indefinite, we affirm the district court's judgment of anticipation as to that patent. Because the district court correctly construed the claims of the '830 patent, under which the patent is not infringed, we affirm the judgment of noninfringement. The case is remanded.

BACKGROUND

Enzo's patents-in-suit are directed to various techniques for labeling and detecting nucleic acids, such as DNA and RNA. To put the analysis in context, we begin with a brief discussion of the basic technology and vocabulary related to this case and undisputed by the parties.

I. Basic Technology and Vocabulary

DNA and RNA are composed of a series of units, called "nucleotides." Each nucleotide is composed of a nitrogenous base, a pentose sugar, and a phosphate group. The phosphate group of one nucleotide forms a covalent bond with the pentose sugar of an adjacent nucleotide, thereby linking the nucleotides along a "sugar-phosphate backbone." Aside from linking the nucleotide units into a polynucleotide strand, the sugar-phosphate backbone provides structural support for the nitrogenous bases. The bases fall into two categories: pyrimidines and purines. Pyrimidines include cytosine ("C"), thymine ("T"), and uracil ("U"). Purines include adenine ("A") and guanine ("G"). DNA contains the bases adenine, thymine, cytosine, and guanine; RNA also includes adenine, cytosine, and

guanine, but contains the base uracil in place of thymine. Two strands of DNA or RNA having complementary bases will bind, or "hybridize," to form a double-stranded complex, or "hybrid," which is held together by hydrogen bonds between complementary bases. In DNA, adenine on one strand binds to thymine on the other; in RNA, adenine binds to uracil; and in both DNA and RNA, cytosine binds to guanine. The process of forming a double-stranded hybrid is called "hybridization." The reverse process, resulting in two separate strands, is called "denaturation."

Because hybridization occurs in a predictable manner between complementary strands, it is possible to detect the presence of a nucleic acid of interest in a sample. For example, a chemical entity, called a "label," can be attached to or incorporated into a nucleic acid strand of a known sequence, called a "probe," which will hybridize with a complementary sequence of interest, called a "target." Once the probe is hybridized with the target, a detectable signal is generated either from the label itself (referred to as "direct detection") or from a secondary chemical agent that is bound to the label (referred to as "indirect detection"). If a signal is detected from the sample after all unhybridized probes have been removed, detection of the signal implies the presence of a target in that sample.

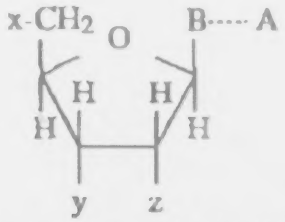
Labeling of nucleic acids has been accomplished using a variety of chemical entities. For example, with radioactive labels, an isotope of hydrogen (^{3}H), phosphorous (^{32}P), or carbon (^{14}C) is substituted for a non-radioactive atom within the probe, and the isotope is then detected using a radiation detector. But radioactive labels have drawbacks. As explained in the '824, '767, and '928 patents, radioactive labels

are "potentially hazardous," "expensive to purchase and use," and "often very unstable." '824 patent col.1 ll.34-45.[1]

To avoid these drawbacks, the inventors of the patents-in-suit developed a series of nucleotide probes that do not rely on traditional radioactive labels. The '824, '767, and '928 patents are directed to these developments and all claim priority to an application filed on April 17, 1981. The '830 patent issued from an application filed on February 26, 1988 and is directed to improvements over some of the probes claimed in the earlier patents.

II. The '824, '767, and '928 Patents

In general, the claims of the '824, '767, and '928 patents are directed to a "compound" (whose structure is depicted below), or a method of using that compound as a detection probe. In this compound, a nitrogenous base "B" is covalently attached, either directly or through a "linkage group" (represented by the dotted line), to a chemical moiety "A."



The "linkage group" is not recited in the independent claims in structural terms. Rather, the linkage group is recited functionally as "not interfering substantially" with both hybridization and detection

[1] Because the '824, '767, and '928 patents share a common specification, we shall cite the '824 patent when referencing the common specification.

('824 and '767 patents) or simply detection ('928 patent). *See* '824 patent col.31 ll.31-34 ("said linkage group not interfering substantially with the characteristic ability of said compound to *hybridize* with said nucleic acid or of A to be *detected*" (emphases added)); '767 patent col.31 ll.2-7 ("a linkage group that does not substantially interfere with the characteristic ability of the oligo- or polynucleotide to *hybridize* with a nucleic acid and does not substantially interfere with formation of the signalling moiety or *detection* of the detectable signal" (emphases added)); '928 patent col.30 ll.29-30 ("said linkage group not interfering substantially with *detection* of A" (emphasis added)). The specification describes the function of the linkage group as follows:

> [I]t is generally preferred that the chemical linkage include an olefinic bond at the α-position relative to B . . . . [Which] serves to hold the moiety A away from the base when the base is paired with another in the well known double-helix configuration. This permits interaction with polypeptide to occur more readily, thereby facilitating complex formation. Moreover, single bonds with greater rotational freedom may not always hold the moiety sufficiently apart from the helix to permit recognition by and complex formation with polypeptide.

'824 patent col.8 ll.54-68.

The chemical moiety A is the label that facilitates detection. In claim 1 of the '824 and '767 patents, moiety A "comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing a detectable signal." In claim 1 of the '928 patent, moiety A "represents at least three carbon atoms and an indicator molecule

selected from the group consisting of fluorescent dyes, electron-dense reagents, enzymes which can be reacted with a substrate to produce a visually detectable reaction product, and radioisotopes."

The symbols "x," "y," and "z" represent, variously, one of the following: hydrogen, hydroxyl, or one or more components of the sugar-phosphate backbone.

III. The '830 Patent

The later-filed '830 patent contains claims to both a compound and a method of detection using that compound. The claimed compound is a nucleotide labeled with "at least one non-radioactive moiety directly or indirectly attached to each of the 5' and 3' end nucleotides thereof." '830 patent col.13 ll.63-65, col.14 ll.58-61. The 5' and 3' positions are locations on a pentose sugar: the 5' end is the so-called "left" end of the polymer; the 3' end is the so-called "right" end of the polymer. In the method claim, a "target" strand is contacted under hybridization conditions with both (i) a "probe" strand having 5' and 3' labels and (ii) a "preformed detectable molecular complex." *Id.* col.14 ll.53-64. Detection is accomplished by "detecting any hybridized complexes." *Id.* col.14 ll.65-66.

IV. Proceedings Below

On June 7, 2004, Enzo sued Applera for infringement of six patents, four of which are here on appeal.[2] The asserted claims of the four patents on appeal are: claims 1, 18, 19, 21, 26, 28, 32, and 33 of the '824 patent; claims 1, 2, 8, 11, 13, 42, 46-51, 67, 68, and 70 of the '767 patent; claims 1 and 2 of the '928 patent; and claims 1, 12, and 18 of the '830 patent.

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[2] The unappealed patents are U.S. Patents No. 4,711,955 and No. 4,994,373.

The district court issued a claim construction ruling on October 12, 2006. *Enzo Biochem, Inc. v. Applera Corp.*, No. 04-929, 2006 WL 2927500 (D.Conn. Oct. 12, 2006) ("*Claim Construction*"). With regard to the linkage group in each of the '824, '767, and '928 patents, the district court construed the "not interfering substantially" language to mean that "the linkage group neither substantially interferes with the ability of the compound to hybridize with the nucleic acid nor substantially interferes with the ability of A to be detected." *Id.* at *6. With regard to the moiety A, the district court found the differing claim language of the '824, '767, and '928 patents to be relevant to whether A constitutes the whole or merely a portion of the entity that produces a detectable signal. More specifically, with regard to the '824 and '767 patents, the district court held that "A may be a part of or the entire signalling moiety," and therefore adopted Enzo's proposed construction that "A comprises at least three carbon atoms and is one or more parts of a signalling moiety, which includes, in some instances, the whole signalling moiety." *Id.* at *4. By contrast, the district court held that the plain language of the '928 patent "precludes a construction where A is the entire [indicator] molecule," and therefore adopted Applera's proposed construction that "A must have at least three carbon atoms and an indicator molecule selected from the group consisting of (i) fluorescent dyes, (ii) electron-dense reagents, (iii) enzymes which can be reacted with a substrate to produce a visually detectable reaction product, or (iv) radioisotopes." *Id.* at *5. Finally, as to the "non-radioactive moiety" of the '830 patent, because the claims call for the use of a "detectable molecular complex," the district court construed "non-radioactive moiety" to mean "a moiety that is utilized in indirect detection, i.e., a moiety

that can be detected with a preformed detectable molecular complex." *Id.* at *11.

Enzo conceded that under the district court's construction it could not prove infringement of the '830 patent. Based on this concession, the district court granted summary judgment of noninfringement of the '830 patent on August 7, 2007. Applera then moved for summary judgment of invalidity of all asserted claims of the '824, '767, and '928 patents based on: (1) lack of written description under 35 U.S.C. § 112, ¶ 1; (2) lack of enablement under 35 U.S.C. § 112, ¶ 1; (3) indefiniteness under 35 U.S.C. § 112, ¶ 2; and (4) anticipation under 35 U.S.C. § 102.

On September 6, 2007, the district court denied Applera's summary judgment motion as to lack of written description and enablement, but granted the motion as to indefiniteness and anticipation. *Enzo Biochem, Inc. v. Applera Corp.*, No. 3:04-CV-929, 2007 WL 2669025 (D.Conn. Sept. 6, 2007) ("*Summary Judgment*"). With regard to indefiniteness, the district court held that the "not interfering substantially" language in the asserted claims of all three patents is indefinite because "[t]he specifications neither set forth how one would gauge substantial interference, nor delimit the threshold at which interference with the procedure prevents [the claimed] method from being implemented." *Id.* at *12. Alternatively, the district court found these same claims to be anticipated by at least one of three prior art references.[3] In concluding that there was no genuine issue

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[3] The three prior art references are: Hiroshi Kasai et al., *Specific fluorescent labeling of 7-(aminomethyl)-7-deazaguanosine located in the anticodon of tRNA^{Tyr} isolated from E. coli mutant*, 7 Nucleic Acids Res. 231 (1979) ("Kasai"); Alfred Pingoud et al., *Fluoresceinylthiocarbamyl-tRNA^{Tyr}: a useful derivative of tRNA^{Tyr}*

of material fact that the prior art taught a linkage group that did "not substantially interfere" with hybridization and detection, the district court observed that "[a]lthough this Court has determined that the 'substantially interfere' language in the ['824, '767, and '928 p]atents is the basis for their invalidity, interpretation of the phrase for purposes of anticipation does not affect the invalidity ruling." *Id.* at *13. Thus, on summary judgment, all asserted claims of the '824, '767, and '928 patents were held invalid as either indefinite or anticipated.

The district court entered final judgment with respect to all six patents on March 5, 2009. Enzo appeals the final judgment with respect to the '824, '767, '928, and '830 patents. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

"A determination that a patent claim is invalid for failing to meet the definiteness requirement in 35 U.S.C. § 112, ¶ 2 is a legal question reviewed *de novo*." *Young v. Lumenis, Inc.*, 492 F.3d 1336, 1344 (Fed. Cir.2007). "Because a patent is presumed to be valid, the evidentiary burden to show facts supporting a conclusion of invalidity is one of clear and convincing evidence." *Id.* at 1345. "We review a district court's grant of summary judgment de novo, reapplying the standard applicable at the district court." *Id.* "While anticipation is a question of fact, 'it may be decided

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(E.coli) for physiochemical studies, 4 Nucleic Acids Res. 327 (1977) ("Pingoud"); J.G.J. Bauman, *Cytochemical Detection of Specific Nucleic Acid Sequences Development and Application of In Situ Hybridisation Methods for Fluorescence Microscopy* (doctoral thesis publ. Drukkerji J.H. Pasmans b.v. 's-Gravenhage, Netherlands (1980)) ("Bauman").

on summary judgment if the record reveals no genuine dispute of material fact.'" *Leggett & Platt, Inc. v. VUTEk, Inc.*, 537 F.3d 1349, 1352 (Fed.Cir.2008) (quoting *Golden Bridge Tech., Inc. v. Nokia, Inc.*, 527 F.3d 1318, 1321 (Fed.Cir.2008)). Summary judgment is appropriate "if the pleadings, the discovery and disclosure materials on file, and any affidavits show that there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law." Fed.R.Civ.P. 56(c)(2).

I. The '824, '767, and '928 Patents

Enzo challenges the district court's grant of summary judgment that all asserted claims of the '824, '767, and '928 patents are invalid in the alternative—as indefinite, but if not indefinite, then invalid as anticipated. As a preliminary matter, we observe that a claim cannot be both indefinite and anticipated. A determination that a claim is anticipated involves a two-step analysis: "the first step requires construing the claim," and "[t]he second step in the analysis requires a comparison of the properly construed claim to the prior art . . . . " *Power Mosfet Techs., LLC v. Siemens AG*, 378 F.3d 1396, 1406 (Fed.Cir.2004). If a claim is indefinite, the claim, by definition, cannot be construed. Without a discernable claim construction, an anticipation analysis cannot be performed. *See Honeywell Int'l, Inc. v. Int'l Trade Comm'n*, 341 F.3d 1332, 1342 (Fed.Cir.2003) (vacating finding of infringement entered after claims were properly held to be indefinite).

A. Indefiniteness

On appeal, Enzo first argues that the district court incorrectly determined that the "not interfering substantially" language in the '824, '767, and '928 patents

is indefinite. In Enzo's view, the specifications provide specific examples of linkage groups that do not substantially interfere with hybridization and detection, as well as general criteria for selecting suitable linkage groups. Moreover, Enzo asserts that the specification provides a test for measuring the degree of interference, namely, comparing the thermal denaturation profile (i.e., melting temperature) of a modified polynucleotide with that of an unmodified polynucleotide.

Applera responds that the district court correctly determined that the "not interfering substantially" language is indefinite, arguing that nothing in the patents explains how to measure "interference" or how to determine whether it is "substantial." Because even a minor alteration of a single nucleotide may have profound effects on the ability of a DNA strand to hybridize, depending on the length and sequence of the strand, Applera argues that identical linkage groups may cause interference in some strands but not in others, thus rendering the claims hopelessly ambiguous.

We agree with Enzo that the claims are not indefinite. "Indefiniteness requires a determination whether those skilled in the art would understand what is claimed. To make that determination, we have explained that '[i]n the face of an allegation of indefiniteness, general principles of claim construction apply.'" *Young*, 492 F.3d at 1346 (quoting *Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1348 (Fed.Cir.2005)). "In that regard, claim construction involves consideration of primarily the intrinsic evidence, *viz.*, the claim language, the specification, and the prosecution history." *Id.* When a "word of degree" is used, the court must determine whether

the patent provides "some standard for measuring that degree." *Seattle Box Co., Inc. v. Indus. Crating & Packing, Inc.*, 731 F.2d 818, 826 (Fed.Cir.1984). Similarly, when a claim limitation is defined in "purely functional terms," a determination of whether the limitation is sufficiently definite is "highly dependent on context (e.g., the disclosure in the specification and the knowledge of a person of ordinary skill in the relevant art area)." *Halliburton Energy Servs., Inc. v. M-I LLC*, 514 F.3d 1244, 1255 (Fed.Cir.2008).

Because the claim language of the '824 and '767 patents differs from that of the '928 patent with regard to "hybridization" and "detection," we address these two terms separately.

1. Hybridization

The claims of the '824 and '767 patents provide that the linkage group must not substantially interfere with both hybridization and detection: '824 patent col.31 ll.31-34 ("said linkage group not interfering substantially with the characteristic ability of said compound to *hybridize* with said nucleic acid or of A to be *detected*" (emphases added)); '767 patent col.31 ll.1-7 ("a linkage group that does not substantially interfere with the characteristic ability of the oligo- or polynucleotide to *hybridize* with a nucleic acid and does not substantially interfere with formation of the signalling moiety or *detection* of the detectable signal" (emphases added)). By contrast, the claims of the '928 patent provide only that the linkage group must not substantially interfere with detection: "said linkage group not interfering substantially with *detection* of A." '928 patent col.30 ll.28-30 (emphasis added). The district court, however, adopted an identical construction for all three patents that refers to both hybridization and detection: "the linkage group

neither substantially interferes with the ability of the compound to *hybridize* with the nucleic acid nor substantially interferes with the ability of A to be *detected*." *Claim Construction*, 2006 WL 2927500, at *6 (emphases added).

As a preliminary matter, we see no basis to read a "hybridization" requirement into the claims of the '928 patent. Nothing in the claims refers to hybridization, and neither the specification nor the prosecution history contains a clear disclaimer or a contrary definition regarding the "not interfering substantially" language that would require us to read such a requirement into the claims. The applicants knew how to claim a linkage group that does not substantially interfere with hybridization, as they did in the '824 and '767 patents, but specifically omitted that language from the claims of the related '928 patent. We therefore modify the construction of this limitation with regard to the '928 patent to read: "the linkage group does not substantially interfere with the ability of A to be detected."

With regard to the '824 and '767 patents, the term "hybridization" has a definite meaning. The district court correctly understood the term to mean "the binding of two separate, complementary strands of nucleic acids to form nucleic acid hybrids." *Id.* at *1 n. 1. The ambiguity, in the district court's view, was that a person of ordinary skill would not understand whether a linkage group interferes with hybridization "substantially."

We begin with the language of the claims. The word "substantially," when used in a claim, can denote either language of approximation or language of magnitude. *See Deering Precision Instruments, LLC v. Vector Distrib. Sys., Inc.*, 347 F.3d 1314, 1323 (Fed.Cir.2003).

As used in the phrase "not interfering substantially," the word "substantially" denotes language of magnitude because it purports to describe *how much* interference can occur during hybridization, i.e., an insubstantial amount of interference. *See Epcon Gas Sys., Inc. v. Bauer Compressors, Inc.*, 279 F.3d 1022, 1031 (Fed.Cir.2002) ("[T]he phrase 'substantially below' signifies language of magnitude, i.e., not insubstantial."). The claims in this case provide at least some guidance as to how much interference will be tolerated. A dependent claim in both patents specifies that the linkage group has a particular structure (-CH=CH-CH_2-NH-). *See* '824 patent col.32 ll.66-68; '767 patent col.31 ll.38-40. A person of ordinary skill would presume that a structure recited in a dependent claim will perform a function required of that structure in an independent claim. *See AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234, 1242 (Fed.Cir.2003) ("Under the doctrine of claim differentiation, dependent claims are presumed to be of narrower scope than the independent claims from which they depend."). Thus, it may be presumed that the term "not interfering substantially" in the independent claims allows for at least as much interference as that exhibited when the linkage group has the structure specified in the dependent claims.[4]

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[4] Of course, if this particular embodiment is inoperable, because a linkage group having the structure -CH=CH-CH_2-NH- entirely precludes hybridization, then the basis for invalidity would be a lack of enablement, not indefiniteness. *Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1382 (Fed.Cir.2001) (stating that inoperable embodiments present "an issue of enablement, and not indefiniteness"); *Miles Labs., Inc. v. Shandon Inc.*, 997 F.2d 870, 875 (Fed.Cir.1993) ("The invention's operability may say nothing about a skilled artisan's understanding of the bounds of the claim.").

The specification provides additional examples of suitable linkage groups, including some criteria for selecting them. After stating generally that the linkage group "may include any of the well known bonds including carbon-carbon single bonds, carbon-carbon double bonds, carbon-nitrogen single bonds, or carbon-oxygen single bonds," the specification goes on to note that "[i]t is even more preferred that the chemical linkage group be derived from a primary amine, and have the structure -CH_2-NH-, since such linkages are easily formed utilizing any of the well known amine modification reactions." '824 patent col.8 ll.54-58, col.9 ll.1-5. Moreover, one of the "essential criteria" of a modified polynucleotide noted in the specification is that "the linkage that attaches the probe moiety should withstand all experimental conditions to which normal nucleotides and polynucleotides are routinely subjected, e.g., extended hybridization times at elevated temperatures, phenol and organic solvent extraction, electrophoresis, etc." *Id.* col.6 l.29, col.7 ll.3-8.

The specification also teaches that the polynucleotides' "thermal denaturation profiles and hybridization properties" can be used to measure the degree to which a linkage group interferes with hybridization. *Id.* col.18 ll.61-62. Because hybridization occurs via hydrogen bonding between complementary bases, any interference in this bonding will result in weaker intermolecular forces and thus a lower melting temperature (T_m) of the hybrid. For example, the specification states that a DNA strand was modified by substituting every thymidine residue of the strand with a biotinyl-nucleotide. The resultant hybridization exhibited by the modified DNA strand was reported to be acceptable: "the T_m is *only* 5 °C less than that of the unsubstituted control." *Id.* col.19 ll.5-8 (emphasis

added). A similar test was performed on poly d(A-bioU), in which every base pair contained a bio-dUMP residue. This modified polynucleotide showed a significantly lower T_m than the unsubstituted control, yet its hybridization was still deemed acceptable: "Although the T_m . . . is 15 °C lower than the poly d(A-T) control, the *degree of cooperativity and the extent of hyperchromicity* observed both during denaturation and renaturation *were the same* for the two polymers." *Id.* col.19 ll.9-14 (emphases added). Thus, as a general guideline, when a linkage group is incorporated into a DNA strand having a length and sequence similar to those used in the specification, a decrease in T_m of up to 5 °C implies that the linkage group does not "substantially interfere" with hybridization, and a decrease of up to 15 °C is acceptable if the degree of cooperativity and the extent of hyperchromicity are the same for the modified and unmodified strands.

The prosecution history of these patents is also helpful. Before the U.S. Patent and Trademark Office ("PTO"), Enzo overcame an indefiniteness rejection over the "not interfering substantially" language by submitting a declaration under 37 C.F.R. § 1.132, which was signed by its vice president, Dr. Engelhardt ("Engelhardt Declaration"), listing eight specific linkage groups that Enzo declared did not substantially interfere with hybridization or detection. Among the named linkage groups was $-CH=CH-CH_2-NH-$ (the same group recited in the patents' dependent claims) and $-NH-(CH_2)_6-NH-$ (a new group that is not found in the specification and which contains only single bonds). J.A. 4320. Based on this submission, the examiner withdrew the indefiniteness rejection.

Because the intrinsic evidence here provides "a general guideline and examples sufficient to enable a

person of ordinary skill in the art to determine [the scope of the claims]," *In re Marosi*, 710 F.2d 799, 803 (Fed.Cir.1983), the claims are not indefinite even though the construction of the term "not interfering substantially" defines the term without reference to a precise numerical measurement, *see Young*, 492 F.3d at 1346 (holding that a word of degree was definite, even without a numerical claim construction); *Exxon*, 265 F.3d at 1381 (same); *Marosi*, 710 F.2d at 803 (same); *In re Mattison*, 509 F.2d 563, 565 (CCPA 1975) (same). When deciding whether a particular linkage group is or is not "substantially" interfering with hybridization within the meaning of the district court's construction, a person of ordinary skill would likely look to the thermal denaturation profiles and hybridization properties (including T_m) of the modified nucleotide, to see whether they fall within the range of exemplary values disclosed in the intrinsic evidence. *See Young*, 492 F.3d at 1346 (stating that a figure in the specification "provides a standard for measuring the meaning of the term 'near,'" even without a numerical claim construction); *Exxon*, 265 F.3d at 1380 (stating that a "period sufficient," recited in the claim, can be ascertained by performing activity checks).

Contrary to Applera's assertion, the fact that the binding strength of a DNA strand may vary, based on the length and sequence of the strand, does not mean that the choice of a linkage group will "depend solely on the unrestrained, subjective opinion of a particular individual purportedly practicing the invention," as in *Datamize*, 417 F.3d at 1350. In *Datamize*, the invention was directed to a computer interface screen with an "aesthetically pleasing look and feel." *Id.* at 1344-45. The patentee sought a construction of the term "aesthetically pleasing" that depended solely on

the subjective opinion of the person selecting features to be included on the interface screen. Nothing in the intrinsic evidence provided any guidance as to what design choices would result in an "aesthetically pleasing" look and feel. *Id.* at 1352. The claims were held indefinite because the very same interface screen may be "aesthetically pleasing" to one user but not to another.

Here, by contrast, the binding strength of a DNA strand will depend on the length and sequence of the strand, not on the subjective opinion of the particular chemist performing the hybridization. This is because, under a given set of experimental conditions, a DNA strand of a given length and sequence will have a fixed, measurable denaturation profile, which can be compared with the examples in the specification to determine whether interference with hybridization is substantial. The claims are not indefinite simply because the binding strength of a DNA strand will vary based on the strand's length and sequence. *See Young*, 492 F.3d at 1346 (holding claim definite even though "the size of the appendage and the amount of skin required to be incised will vary from animal to animal based on the animal's size").

Thus, we hold that the claim language regarding "hybridization" is not indefinite.

2. Detection

With regard to "detection," we agree with Enzo that the claims are not indefinite for most of the same reasons discussed in connection with "hybridization." The eight linkage groups listed in the Rule 132 declaration were said not to "interfere[ ] with the ability of biotin in an oligo- or polynucleotide probe of this invention to form a detectable complex with one

of avidin, streptavidin or antibodies to biotin or iminobiotin." J.A. 4318. According to the specification, when biotin is used as the moiety A, the resultant complexes can be detected "by means of conventional detection techniques." '824 patent col. 18 ll.4-6. So long as moiety A can be detected within the level of detection achieved by the applicants using the exemplary linkage groups disclosed in the intrinsic evidence, a person of ordinary skill would understand that a different linkage group (one that is not disclosed in the intrinsic evidence) likewise does not "substantially interfere" with the detection of moiety A. The claims are not indefinite even if some experimentation is required to determine the exact level of detection achieved by the applicants using their exemplary linkage groups. *See Exxon*, 265 F.3d at 1379 ("Provided that the claims are enabled, and no undue experimentation is required, the fact that some experimentation may be necessary to determine the scope of the claims does not render the claims indefinite.").

* * *

For the foregoing reasons, we conclude that the "not interfering substantially" language in the '824, '767, and '928 patents is not indefinite.

B. Anticipation

The district court granted Applera's motion for summary judgment that (1) Kasai anticipates the asserted claims of the '824 and '767 patents, (2) Pingoud anticipates the asserted claims of the '767 patent, and (3) Bauman anticipates the asserted claims of the '928 patent. On appeal, Enzo argues that none of the references disclose a "linkage group" that does not substantially interfere with hybridiza-

tion, and that the testimony of its expert, Dr. Sherman, was sufficient to create a genuine issue of material fact.

In moving for summary judgment on an issue as to which Applera bore the burden of persuasion, Applera supported its motion with detailed claim charts showing where each and every claim limitation is disclosed in the prior art, and an expert declaration explaining how the prior art meets those limitations under the district court's claim construction. *See Saab Cars USA, Inc. v. United States*, 434 F.3d 1359, 1369 (Fed.Cir.2006) (party with the burden of persuasion on an issue must "provide evidence sufficient, if unopposed, to prevail as a matter of law"); 11 James Wm. Moore, Moore's Federal Practice § 56.13[1] (3d ed. 2009) ("[I]f the movant has the burden of persuasion on an issue, the movant must make a stronger claim to summary judgment by introducing supporting evidence that would conclusively establish movant's right to a judgment after trial should nonmovant fail to rebut the evidence."). With respect to the "linkage group" limitation, two of Applera's prior art references (Kasai and Pingoud) employ a $-CH_2-NH-$ linkage group, which arguably belongs to the set of linkage groups disclosed in the patents-in-suit as "even more preferred" embodiments. '824 patent col.9 ll.1-5 ("It is even more preferred that the chemical linkage group be derived from a primary amine, and have the structure $-CH_2-NH-$, since such linkages are easily formed utilizing any of the well known amine modification reactions."). Moreover, all three of Applera's references, on their face, report the ability to detect the presence of moiety A. If unopposed, this evidence would entitle Applera to judgment as a matter of law. We therefore agree with

the district court that Applera carried its initial burden of making a prima facie showing of anticipation.

"When a motion for summary judgment is properly made and supported, an opposing party may not rely merely on allegations or denials in its own pleading; rather, its response must—by affidavits or as otherwise provided in this rule—set out specific facts showing a genuine issue for trial." Fed.R.Civ.P. 56(e)(2). The requirement that the nonmovant must set forth "specific facts" means that "[m]ere denials or conclusory statements are insufficient" to survive summary judgment. *Barmag Barmer Maschinenfabrik AG v. Murata Machinery, Ltd.*, 731 F.2d 831, 836 (Fed.Cir.1984). The standard on this issue is the same in the Second Circuit, *see Davis v. New York*, 316 F.3d 93, 100 (2d Cir.2002), which applies in this case "because the issue is a procedural matter not unique to patent law." *Arthur A. Collins, Inc. v. N. Telecom Ltd.*, 216 F.3d 1042, 1048 (Fed.Cir.2000).

After reviewing the material that Enzo submitted in opposition to Applera's summary judgment motion, we conclude that Enzo has raised a genuine issue of material fact as to Kasai and Pingoud sufficient to survive summary judgment of anticipation of the '767 and '824 patents. However, as discussed below, Enzo has failed to raise a genuine issue of material fact with respect to Bauman and the '928 patent.

1. Kasai

With respect to Kasai, Enzo offered the declaration of its expert, Dr. Sherman, who stated that Kasai's "aminomethyl group [(-CH_2-NH-)] would not provide sufficient rigidity to prevent significant interference with hybridization of a complementary polynucleotide. Indeed, one would predict based on the flexibility of

this functional group and the concomitant high degree of motion, there would be significant interference due to free rotation about the single bonds." Sherman Decl. ¶ 44. This is in contradistinction to a linkage group including a carbon-carbon double bond, which presumably would be sufficiently rigid to prevent significant interference with hybridization, because the bound elements would not be free to rotate about their axes and sterically interfere at the hybridization site.

During prosecution, Enzo submitted the Engelhardt Declaration, which listed eight suitable linkage groups that did not substantially interfere with hybridization or detection. Seven included a carbon-carbon double bond, and one, -NH-$(CH_2)_6$-NH-, consisted entirely of single bonds. Applera argues that Dr. Sherman's declaration cannot be credited because it conflicts with Dr. Engelhardt's declaration that an all-single-bond linkage group was suitable. *See Cleveland v. Policy Mgmt. Sys. Corp.*, 526 U.S. 795, 806, 119 S.Ct. 1597, 143 L.Ed.2d 966 (1999) ("The lower courts . . . have held with virtual unanimity that a party cannot create a genuine issue of fact sufficient to survive summary judgment simply by contradicting his or her own previous sworn statement (by, say, filing a later affidavit that flatly contradicts that party's earlier sworn deposition) without explaining the contradiction or attempting to resolve the disparity."). Applera would have us agree with the district court that Dr. Sherman's declaration did not raise a genuine issue of material fact because he "offer[ed] no support, experimental, literary, or otherwise, for [his] assertion" that Kasai would substantially interfere, and that Applera is entitled to summary judgment of anticipation. *See Summary Judgment*, 2007 WL 2669025, at *13.

Applera's argument ignores the standard for summary judgment, which requires that Dr. Sherman's declaration be viewed in a light most favorable to Enzo. *See Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp.*, 149 F.3d 1309, 1315 (Fed.Cir.1998) ("In deciding whether summary judgment was appropriate, we view the evidence in a light most favorable to the party opposing the motion with doubts resolved in favor of the opponent.") (internal citations omitted). Viewing the declaration in a light most favorable to Enzo requires that Dr. Sherman's explanation be read as limited to the specific one-carbon aminomethyl group disclosed in Kasai and not as a sweeping condemnation of single bonds or an unyielding requirement of double bonds. *See* Sherman Decl. ¶ 44 ("[T]he *aminomethyl group* would not provide sufficient rigidity to prevent significant interference with hybridization.") (emphasis added). Dr. Sherman's statement that the aminomethyl group disclosed in Kasai would substantially interfere and Dr. Engelhardt's statement that a six-carbon diamine group would not are not inconsistent, particularly when viewed in a light most favorable to Enzo, as it must be.

Moreover, at least two characteristics of a linkage group contribute to its character as interfering with hybridization or not: the nature of the bonds (i.e., single or double) and the length of the chain. In his declaration, Dr. Sherman chose to focus on the first (the lack of a double bond) in explaining why Kasai would substantially interfere. The '824 patent indicates the preferability of a double bond in the linkage group. '824 patent col.8 ll.58-65 ("[I]t is generally preferred that the chemical linkage include an olefinic [(i.e., double)] bond . . . . [This] serves to hold the moiety A away from the base when the base is paired with another in the well known double-helix

configuration."). *See also* Engelhardt Decl. Ex. A (seven of eight examples incorporate a double bond, including a short three-carbon chain linkage group). However, while Dr. Sherman did not discuss it, the '824 patent also recognizes that the *length* of the linkage group impacts hybridization and detection. *See* '824 patent col.8 ll.65-68 ("Moreover, single bonds with greater rotational freedom may not always hold the moiety *sufficiently apart from the helix* to permit recognition by and complex formation with [a] polypeptide.") (emphasis added). It is elementary stereochemistry that a longer linkage group could hold the moiety farther from the hybridization site than a shorter one. Viewed with this understanding of the technology, the declaration of Dr. Engelhardt cannot be said to obviate the genuine issue of material fact raised by Dr. Sherman's declaration.

Applera also argues that because Kasai's -CH_2-NH- linkage group is within the group of "even more preferred" embodiments, it cannot substantially interfere. However, there are an infinite variety of linkage groups "derived from a primary amine, [with] the structure -CH_2-NH-," *see* '824 patent col.9 ll.1-15, which suggests that not every "even more preferred" linkage group would satisfy the not substantially interfering element. Further, Enzo argues that the "even more preferred" language is properly read as describing a subset of the preferred embodiments—i.e., those with carbon-carbon double bonds at the α-positition—such that the most preferred embodiments have both a carbon-carbon double bond at the α-position, *and* are derived from a primary amine and include a -CH_2-NH- group. The examples in the specification of the most preferred embodiment have both a carbon-carbon double bond at the α-position and an aminomethyl group. '824 patent col. 9 ll.8-16.

Enzo's reading is reasonable, and should have been credited on summary judgment.

For the reasons stated, we reverse the district court's grant of summary judgment of invalidity of the asserted claims of the '824 and '767 patents as anticipated by Kasai.

2. Pingoud

Applera presents two arguments that Pingoud anticipates the '767 patent. First, it relies on a statement by its expert, Dr. Kricka, that "Pingoud was able to detect the label without apparent difficulty, so to the extent Enzo contends that the mere ability to detect a label is sufficient to satisfy this claim limitation presumably they would not dispute that Pingoud satisfies this claim limitation as well." Kricka Decl. ¶ 84, App. A at 60. Second, Applera repeats its argument that Pingoud belongs to the set of compounds described as "even more preferred" in the patents.

Neither argument is sufficient to sustain summary judgment. On its face, Pingoud notes that there was substantial interference with hybridization. Pingoud at 327 ("Codon-anticodon interaction . . . is severely affected by the [fluorescent labeling] modification."). "Codon-anticodon interaction" is indicative of hybridization, and "severely affected" suggests substantial interference. Dr. Sherman recognized this, and, unlike Dr. Kricka, opined that "there would be substantial interference" by the compound disclosed in Pingoud. Sherman Decl. at ¶¶ 61-62. Thus there is a genuine issue of material fact as to whether the Pingoud linkage group substantially interferes with hybridization.

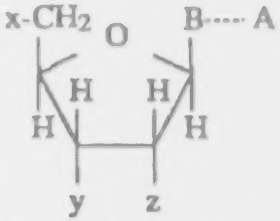
We reject Applera's "most preferred embodiment" argument for the same reasons discussed above in regard to Kasai.

Therefore, we reverse the district court's grant of summary judgment of anticipation of the asserted claims of the '767 patent based on Pingoud.

3. Bauman

Enzo's argument with regard to Bauman is insufficient to raise a genuine issue of material fact. Bauman employs a mercury glutathione linkage group to attach moiety A to base B. However, instead of attaching the linkage group before hybridization, Bauman first performs hybridization and then attaches the linkage group, along with moiety A, to the hybrid. Once attached, moiety A is detected by fluorescence. Because Bauman performs hybridization *before* labeling the polynucleotide, Enzo argues that Bauman cannot anticipate the asserted claims of the '928 patent. In Enzo's view, the claims "require that the linkage group not interfere *after* the label is attached." Reply Br. of Pl.-Appellants 23. We disagree.

First, the claims of the '928 patent are directed to a product, not a process. More specifically, independent claims 1 and 2 are simply directed to a "compound" having the structure:



It is irrelevant, for purposes of anticipation, what method is used, much less what order of steps is used, to attach both moiety A and the linkage group

to base B. *See In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir.1985) ("The patentability of a product does not depend on its method of production.").

Second, as we have already explained, the "not interfering substantially" language in the '928 patent is silent as to hybridization. All that is required of this particular linkage group is that it not substantially interfere with the ability of A to be detected. Enzo does not dispute that Bauman discloses a linkage group that does not substantially interfere with the ability of A to be detected.

Because the district court correctly held that Enzo failed to raise a genuine issue of material fact with respect to Bauman, we affirm the judgment of anticipation as to claims 1 and 2 of the '928 patent.[5]

II. The '830 Patent

The district court construed the term "non-radioactive moiety" in the '830 patent to mean "a moiety that is utilized in indirect detection, i.e., a moiety that can be detected with a preformed detectable molecular complex." *Claim Construction*, 2006 WL 2927500, at *11. Enzo would like the term construed simply to mean "a non-radioactive detection moiety." Thus, under Enzo's proposed construction, the moiety could be utilized in either indirect detection

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[5] Because Bauman anticipates claims 1 and 2 of the '928 patent under the district court's narrower construction of moiety A, wherein A represents only a portion and not the entirety of the indicator molecule, Bauman would necessarily anticipate these claims if, as Enzo argues, A is broad enough to represent either a portion or the entirety of the indicator molecule. Because it would not change the result in this case, we decline to address Enzo's claim construction argument with regard to moiety A.

(wherein the preformed detectable molecular complex is the thing that generates a detectable signal) or direct detection (wherein the non-radioactive moiety is itself the thing that generates a detectable signal). We agree with the district court's construction.

Claims 1, 12, and 18 are independent claims. Claim 14 is a multiple dependent claim that refers back to claims 1 and 12. The claims recite, with key term emphasized:

> 1. An oligo- or polynucleotide having at least one *non-radioactive moiety* directly or indirectly attached to each of the 5' and 3' end nucleotides thereof.
>
> 12. An oligo- or polynucleotide having at least one *non-radioactive moiety* directly or indirectly attached to each of the 5' and 3' terminal nucleotides external to a target hybridization region of said oligo- or polynucleotide.
>
> 14. A nucleic acid hybridization assay composition comprising an oligo- or polynucleotide of claims 1 or 12, and a preformed detectable molecular complex.
>
> 18. A method for detecting a target nucleic acid sequence in a sample comprising:
>
> rendering the nucleic acid in said sample in single-stranded form;
>
> contacting said single-stranded nucleic acid under hybridizing conditions with (i) an oligo- or polynucleotide probe having at least one *non-radioactive moiety* directly or indirectly attached to each of the 5' and 3' end nucleotides thereof, said probe being capable of hybridizing to said

target nucleic acid sequence, and (ii) a preformed detectable molecular complex; and

detecting any hybridized complexes, thereby detecting the target nucleic acid sequence.

Enzo concedes that the term "non-radioactive moiety" cannot be given its literal meaning (i.e., a molecular substructure not labeled with a radioisotope), since the claims would then encompass any piece of natural DNA, rendering the claims invalid on their face. The district court therefore looked to the specification, which contains no disclosure of direct detection but instead refers to an "analyte-specific moiety" detected using "detectable molecules." '830 patent col.3 ll.41-53. Because all detectable molecules mentioned in the specification are those relating to detection via a "preformed detectable molecular complex," the district court concluded that a "non-radioactive moiety" must be detected via a signal generated from the preformed detectable molecular complex rather than from the moiety itself. On appeal, Enzo faults the district court for equating "non-radioactive moiety" with "analyte-specific moiety," and argues that the specification instead equates "non-radioactive moiety" simply with "labeling" of nucleic acids using "labeling moieties." *Id.* col.1 ll.8-11. But even if a non-radioactive moiety is simply a "label," as Enzo suggests, this still leaves open the question whether the non-radioactive moiety is itself capable of generating a detectable signal or whether the preformed detectable molecular complex is what generates the signal.

The claim language strongly suggests that the non-radioactive moiety serves simply as a binding site for a preformed detectable molecular complex, and that the signal is generated by the complex, not the moiety.

Independent claim 18 is unambiguously limited to indirect detection via "a preformed detectable molecular complex." *Id.* col.14 ll.63-64. If the non-radioactive moiety were itself the thing that generated a detectable signal, then there would be no reason to contact it with the preformed detectable molecular complex, as required in part (ii) of the "contacting" step of claim 18. Moreover, in the last step of this claim, what is detected is "any hybridized *complexes*," not the moiety. *Id.* col.14 l.65 (emphasis added). Thus, at least with regard to claim 18, the "non-radioactive moiety" is a moiety that can be detected with a preformed detectable molecular complex. Enzo has not argued that the "non-radioactive moiety" should have a different meaning in independent claim 18 than in independent claims 1 and 12. Indeed, we have recognized that "claim terms are normally used consistently throughout the patent." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir.2005) (en banc).

Referring to the claim language, Enzo argues that the district court's construction of "non-radioactive moiety" violates the doctrine of claim differentiation. Under this doctrine, "the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1315. Because dependent claim 14 adds "a preformed detectable molecular complex" to claim 1, Enzo asserts that the district court's construction of "non-radioactive moiety"—which refers to detection with "a preformed detectable molecular complex"—renders the two claims coextensive. But the district court's construction imposes no requirement that a preformed detectable molecular complex is actually present in claim 1; rather, it simply requires the "non-radioactive moiety"

to be capable of performing a function: "*can* be detected with a preformed detectable molecular complex." *Claim Construction*, 2006 WL 2927500, at *11 (emphasis added). Claim 1, unlike claim 14, is infringed even in the absence of a preformed detectable molecular complex. *See Revolution Eyewear, Inc. v. Aspex Eyewear, Inc.*, 563 F.3d 1358, 1370 (Fed. Cir.2009) (holding that a component of an accused device meets "capable of engaging" limitation even though device is not designed or sold with component in engaging configuration). Because claim 1 is broader than claim 14 under the district court's construction, this case simply does not implicate the doctrine of claim differentiation.

The specification lends no support to Enzo's proposed construction because it contains no disclosure whatsoever of direct detection. This fact alone is not dispositive, of course, because "it is improper to read limitations from a preferred embodiment described in the specification—even if it is the only embodiment—into the claims absent a clear indication in the intrinsic record that the patentee intended the claims to be so limited." *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 913 (Fed.Cir.2004). But, as already discussed, the claim language strongly suggests that the non-radioactive moiety must have the capability of being indirectly detected with a detectable molecular complex.

The prosecution history is not to the contrary. Enzo overcame an obviousness rejection by stating:

> Prior to the instantly claimed invention, no mention or suggestion was ever made regarding the attachment (directly or indirectly) of at least one non-radioactive moiety, e.g., biotin or a biotin analogue, to each of the 5' and 3' end nucleotides

> of an oligo- or polynucleotide. Furthermore, no prior art reference ever taught or suggested the possibility of a nucleic acid hybridization assay composition comprising such a *labelled oligo- or polynucleotide and a preformed detectable complex*, e.g., a preformed avidin or streptavidin detectable molecular complex, as defined by the present claims.

J.A. 307 (emphasis added). On appeal, Enzo argues that this statement supports its proposed construction because it equates a "non-radioactive moiety" with a "labeled oligo- or polynucleotide," which in turn suggests that the moiety is simply a "label." But again, the question is how this "label" is detected. The very same sentence that refers to the claimed compound as a "labelled oligo- or polynucleotide" also refers to a "preformed detectable complex," suggesting that detection is accomplished by the latter. Indeed, the unique binding of a biotin moiety with an avidin complex, referenced in this passage, is an example of indirect detection. Moreover, these prosecution statements were made with regard to all rejected claims standing or falling together, and were not directed to any dependent claim reciting a detectable molecular complex as an express limitation of the claim. All of this suggests that the non-radioactive moiety must be capable of indirect detection with a preformed detectable molecular complex. The prosecution history thus tends to undercut, rather than support, Enzo's proposed construction.

For the foregoing reasons, we affirm the district court's construction of "non-radioactive moiety." Because Enzo stipulated that it cannot prove infringement under this construction, we affirm the judgment of noninfringement of the '830 patent.

CONCLUSION

We reverse the district court's grant of summary judgment that the asserted claims of the '824 and '767 patents are invalid as indefinite and anticipated by Kasai and further that the asserted claims of the '767 patent are anticipated by Pingoud. We affirm the judgment that the '928 patent is invalid as anticipated. We affirm the judgment that the '830 patent is not infringed. The case is remanded for further proceedings consistent with this opinion.

APPENDIX B

UNITED STATES DISTRICT COURT
D. CONNECTICUT

No. 3:04cv929 (JBA)

ENZO BIOCHEM, INC. *et al.*,
Plaintiffs,

v.

APPLERA CORP. *et al.*,
Defendants.

Sept. 6, 2007

RULING ON DEFENDANT APPLERA'S MOTION FOR SUMMARY JUDGMENT OF INVALIDITY [DOC. # 182]

JANET BOND ARTERTON, U.S.D.J.

Plaintiffs Enzo Biochem, Inc., Enzo Life Sciences, Inc., and Yale University (collectively "Enzo") allege patent infringement under 35 U.S.C. §§ 271, *et seq.* against defendants Applera Corp. ("Applera") and Tropix Inc. ("Tropix") with respect to three of four "Ward Patents," specifically Claims 1, 18, 19, 21, 26, 28, 32, and 33 of U.S. Patent No. 5,328,824 ("'824 Patent"); Claims 1, 2, 8, 11, 13, 42, 46, 47, 48, 49, 50, 51, 67, 68, and 70 of Patent No. 5,449,767 ("'767 Patent"); and Claims 1 and 2 of Patent No. 5,476,928 ("'928 Patent"). (*See* Compl. [Doc. # 1] at 1; Def. Reply

Mem. [Doc. # 224] at 2 n. 1.)[1] Defendant Applera now moves for summary judgment of invalidity as to these Ward patents on grounds of failure to satisfy the written description and enablement requirements of 35 U.S.C. § 112 ¶ 1, failure to satisfy the claim definiteness requirement of 35 U.S.C. § 112 ¶ 2, and anticipation under 35 U.S.C. § 102. For the reasons that follow, defendant Applera's Motion will be GRANTED.

I. *Factual Background*

As set out in the Court's Claim Construction Ruling, the Ward patents disclose a method of non-radioactive labeling for detecting the presence of DNA or RNA in a sample. *See Enzo Biochem, Inc. v. Applera Corp.*, No. 3:04cv929 (JBA), 2006 U.S. Dist. LEXIS 74570 (D.Conn. Oct. 12, 2006) ("Claim Construction Ruling"). This method of labeling is effected via the formation of a complex between hybridized nucleotides and a detectable polypeptide. The Ward Patents, which share a specification, are based on a single application filed April 17, 1981 on behalf of then Yale professor Dr. David Ward and two colleagues. The first Ward Patent, the '955 Patent, *see supra* n. 1, issued in 1981; an overview of the asserted claims is provided below.

A. *'824 Patent*

The '824 Patent, which issued on July 12, 1994, discloses a two-step process by which a probe is hybridized with an analyte and then detected as a means of determining the existence of a particular analyte in the sample. Of the asserted claims of this Patent, independent Claim 1 is representative:

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[1] Plaintiffs no longer press their claims related to Patent No. 4,711,955 ("'955 Patent").

A method of detecting the presence or absence of a nucleic acid in a sample which comprises the steps of

(a) contacting under hybridizable conditions said sample with at least one compound comprising the structure: [DIAGRAM]

[. . . .]

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing a detectable signal;

wherein B and A are covalently attached directly or indirectly through a linkage group, said linkage group not interfering substantially with the characteristic ability of said compound to hybridize with said nucleic acid or of A to be detected;

wherein if B is 7-deazapurine, A is attached to the 7-position thereof, and if B is pyrimidine, A is attached to the 5-position thereof;

wherein m, n and p are integers, provided that m and p are not simultaneously 0 and provided further n is never 0; and

wherein z represents H- or HO-; and

(b) detecting said compound or compounds so as to detect said nucleic acid.

('824 Patent, Pls. Ex. 6.) Dependent Claims 18, 19, 21, 26, 28, 32, and 33 describe the structure of the A moiety, indicator molecule B, and the nucleic acid disclosed in Claim 1.

B. *'767 Patent*

The '767 Patent issued on September 12, 1995 and discloses a particular nucleotide useful in hybridization. Plaintiffs allege infringement of independent Claims 1, 42, and 48, and numerous dependent claims. Claim 48 is representative:

> An oligo- or polynucleotide containing therein a sugar moiety having the structure: [DIAGRAM]
>
> [. . . .]
>
> wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing a detectable signal; and
>
> wherein B and A are covalently attached directly or through a linkage group that does not substantially interfere with the characteristic ability of the oligo- or polynucleotide to hybridize with a nucleic acid and does not substantially interfere with formation of the signalling moiety or detection of the detectable signal, provided also that if B is a 7- deazapurine, A or the linkage group is attached to the 7-position of the deazapurine, and if B is pyrimidine, A or the linkage group is attached to the 5-position of the pyrimidine.

('767 Patent, Pls. Ex. 5.) Dependent claims 49, 50, 51, 67, 68, and 70 are directed to the structure of the sugar moiety or of A. Independent Claims 1 and 42 share much of the language in Claim 48, except that Claim 1 discloses that the oligo- or polynucleotide contains a "nucleotide" rather than a sugar moiety, and Claim 42 discloses an "oligo- or polynucleotide sequence comprising at least one of a moiety having the structure: -BA."

C. '928 Patent

Issued on December 19, 1995, the '928 Patent discloses a compound useful as a probe to detect the presence of and/or localize specific polynucleotide sequences. Independent Claim 1 is representative:

> A compound useful as a probe for detecting the presence or absence of a nucleic acid, said compound having the structure: [DIAGRAM]
>
> [. . . .]
>
> wherein A represents at least three carbon atoms and an indicator molecule selected from the group consisting of fluorescent dyes, electron-dense reagents, enzymes which can be reacted with a substrate to produce a visually detectable reaction product, and radioisotopes;
>
> wherein B and A are covalently attached directly or through a linkage group, said linkage group not interfering substantially with detection of A;
>
> wherein if B is a purine, A is attached to the 8-position of the purine, if B is a 7-deazapurine, A is attached to the 7-position of the deazapurine, and if B is a pyrimidine, A is attached to the 5-position of the pyrimidine; and
>
> wherein each of x, y and z represents: [DIAGRAM].

('928 Patent, Pls. Ex. 4.) Independent Claim 2, the only other Claim asserted by Enzo, is substantially similar to Claim 1, except that it discloses that "one of x and y represents [DIAGRAM] and the other of x and y is absent or represents -OH or -H" and that "z represents H- or HO-."

The Court's Claim Construction Ruling construed certain terms relevant to the claims on the instant Motion. First, the '824 and '767 Patents were construed to "cover both direct and indirect detection," *Enzo Biochem*, 2006 U.S. Dist. LEXIS 74570 at 9, on the basis that "A comprises at least three carbon atoms and is one or more parts of a signaling moiety, which includes, in some instances, the whole signaling moiety." Second, the terms "linkage group not interfering substantially with" and "linkage group that does not substantially interfere with" in all of the asserted independent claims were construed to mean that "the linkage group neither substantially interferes with the ability of the compound to hybridize with the nucleic acid nor substantially interferes with the ability of A to be detected," *id.* at 16-17.

II. *Summary Judgment and Invalidity Standards*

Summary judgment is appropriate under Federal Rule of Civil Procedure 56(c) when the moving party establishes that there is no genuine issue of material fact to be resolved at trial and that the moving party is entitled to judgment as a matter of law. *See Celotex Corp. v. Catrett*, 477 U.S. 317 (1986). Materiality is determined by the substantive law that governs the case. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986). "Where the record taken as a whole could not lead a rational trier of fact to find for the nonmoving party, there is no genuine issue for trial." *Matsushita Elec. Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 586 (1986).

"A defendant need not prove a negative when it moves for summary judgment on an issue that the plaintiff must prove at trial. It need only point to an

absence of proof on plaintiff's part, and, at that point, plaintiff must 'designate specific facts showing that there is a genuine issue for trial.'" *Parker v. Sony Pictures Entm't, Inc.*, 260 F.3d 100, 111 (2d Cir.2001), quoting *Celotex*, 477 U.S. at 324.

A patent is presumed valid, as are the individual claims of a patent. 35 U.S.C. § 282. The party claiming invalidity bears "the burden to show the invalidity of the claims by clear and convincing evidence as to underlying facts." *Rockwell Int'l Corp. v. United States*, 147 F.3d 1358, 1364 (Fed.Cir.1998). This standard demands evidence that proves in the mind of the trier of fact "an abiding conviction that the truth of [the] factual contentions are 'highly probable.'" *Intel Corp. v. Int'l Trade Comm'n*, 946 F.2d 821, 829-30 (Fed Cir.1991) (affirming determination that patent not invalid where "extensive inference" from evidence did not meet the clear and convincing standard).

III. *Discussion*

A. *Written Description Requirement*

The first of defendant's summary judgment grounds is that Patents '824 and '767 are invalid under Patent Act § 112 ¶ 1, which requires that a specification "contain a written description of the invention, and of the manner and process of making and using it, in . . . full, clear, concise, and exact terms," 35 U.S.C. § 112 ¶ 1. According to Applera, although Patents '824 and '767 have been construed by the Court to cover both direct and indirect detection, the specification inadequately describes a system for direct detection.

In order to satisfy the written description requirement, the specification must show that the applicant possessed the invention as of the filing date, *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed.Cir.1991), thus ensuring that "the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification," *Reiffin v. Microsoft Corp.*, 214 F.3d 1342, 1345 (Fed.Cir.2000). The written description may be accomplished "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed instruction." *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed.Cir. 1997). "While it is legitimate to amend claims or add claims to a patent application . . . there must be support for such amendments or additions in the originally filed application." *PIN/NIP, Inc. v. Platte Chem. Co.*, 304 F.3d 1235, 1247 (Fed.Cir. 2002). "The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence." *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed.Cir.2005). A claim is not invalidated simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed.Cir.2006).

In contesting whether the specification teaches direct detection, defendant makes several arguments. First, Applera focuses on the "A" moiety, which is defined in the specification as follows:

> A represents a moiety consisting of at least three carbon atoms which is capable of forming a detectable complex with a polypeptide when the

> compound is incorporated into a double-stranded ribonucleic acid, deoxyribonucleic acid duplex, or DNA-RNA hybrid;

'824 Patent 7:26-30.[2] Defendant contends that the specification discusses the "A" moiety as capable of only indirect detection, meaning that direct detection was not possessed by Enzo when the Ward Patents issued, and that the disclosed labels are described in reference to indirect detection.

Applera is correct that the specification repeatedly references "A"'s capability of "forming a detectable complex with a polypeptide ('824 Patent 3:49-50, 5:33-34, 7:26-27, 8:4-5, 11:16-17; 16:66-67), and describes "A" (in the form of disclosed labels biotin, iminobiotin, and various haptens) as "interacting with appropriate antibodies to produce complexes" (*id.* at 8:12-13) or as "coupled to potentially demonstrable indicator molecules" (including the fluorescent dyes fluorscein and rhodamine) to be used in detection of a biotin probe (*id.* at 18:7-17). According to defendant's expert Larry J. Kricka, "[t]he specification repeatedly and exclusively discloses that the 'A' moiety is detected not by itself, but by complexing it with a labeled (and thus detectable) polypeptide to form a complex that generates a detectable signal." (Kricka Decl. [Doc. # 183] ¶ 107.) He observes that "[e]ach disclosure in the specification of 'indicator molecules' explicitly describes such molecules as being coupled to a detector protein—an entity that is used to detect the 'A' moeity—and not to the 'A' moiety itself." (*Id.* ¶ 110.) Plaintiffs respond to these portions of the specification by arguing that because direct

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[2] Because the specification is identical for all of the Ward Patents, the Court will cite only to the '824 Patent for consistency.

detection methods using fluorescent dyes and other single-component signaling systems were known when the Ward specification was filed, the specification's disclosure of labeled nucleotides suitable for incorporation into polynucleotides is sufficient, and, more importantly, that Example 9 of the specification discloses direct detection.

While Examples 1 through 6 undisputedly disclose only indirect detection methods (Sinden Supplem. Expert Report, Pls. Ex. 3, ¶ 15), Enzo's expert witness Richard R. Sinden opines that Example 9, particularly in the context of Examples 7 and 8, "disclose[s] techniques that involve detection where A is the whole of the signalling moiety" (*id.* ¶ 10). Examples 7 and 8, entitled "Synthesis of NAGE-UTP and NAGE-dUTP," describe the method for synthesizing the linker arm NAGE, which can be attached to UTP and dUTP nucleotides. (*Id.* ¶ 11; '824 Patent at 28-29.) Example 9 sets out "Karyotyping," "Diagnosis of Genetic Disorders," and "Microorganism Detection and Identification" as "Uses of Labeled DNA Sequences." ('824 Patent at 29-30.) Sinden reads Example 9 as invoking the labeling procedures in Examples 7 and 8 and providing for direct detection methods using fluorescent dyes: he interprets the phrase "adding a fluorescent stain to the label" in Example 9 as denoting attachment of a fluorescent dye to the available amine group of the NAGE linker from Examples 7 and 8, and not the addition of biotin with subsequent detection using a linked indicator as in indirect detection Examples 1 through 6. (Sinden Supplem. Expert Report, Pls. Ex. 3, ¶ 13.) Indirect detection using biotin as compatible with Examples 1 through 6 would lead to background interference or distort detection results, Sinden opines. (*Id.* ¶ 15.)

Moreover, Sinden points to Example 9's allowance for "two sets of labels," a condition he claims is specific to the direct detection context. (*Id.* ¶ 16.)

Applera's expert Kricka, in contrast, claims that Example 9 simply elaborates on uses for labeled sequences set out in the preceding eight examples, all of which describe indirect detection methods. He quotes from the karyotyping section of Example 9, and reads it as exclusively describing indirect detection:

> polynucleotides are hybridized with chromosomal deoxyribonucleic acid and the resulting duplexes contact with appropriate polypeptides under suitable conditions to permit complex formation. The polypeptides include detectable moieties so that the location of the complexes can be determined and the location of specific genes thereby fixed.

Id. at ¶ 113, quoting '824 patent at 24:40-50. In addition, Applera further points to a paper published by two of the Ward Patents' inventors, David Ward and Pennina R. Langer-Safer, in 1982 that discloses a method of performing the procedures in Example 9 using only indirect labels, as well as to a 1990 paper by Ward on using multiple probes labeled with different indirect labels to analyze chromosomes. See Pennina R. Langer-Safer, et al., "Immunological method for mapping genes on Drosophila polytene chromosomes," *Proc. Natl. Acad. Sci. USA*, (1982), Pls. Ex. 7; Ann L. Boyle, *et al.*, "Differential distribution of long and short interspersed element sequences in the mouse genome: Chromosome karyotyping by fluorescence *in situ* hybridization," *Proc. Natl. Acad. Sci. USA* (1990), Pls. Ex. 8. Indeed, Sinden recognizes the two-color analysis method

using indirect detection described in the 1990 paper as "one embodiment" of what is contemplated by Example 9 such that "it is possible to carry out the procedures of Example 9 of the Ward patent using an indirect detection system." Apr. 13, 2006 Sinden Dep., Def. Ex. 9, at 127, 128.)[3]

In *Univ. of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916 (Fed.Cir.2004), the Federal Circuit affirmed a judgment of invalidity for inadequate written description where the functional description of the invention consisted of a bare assertion that the patent covered "'a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product,'" *id.* at 928, without further narrowing its scope by disclosing "just which peptides, polynucleotides, and small organic molecules have the desired characteristic of selectively inhibiting PGHS-2," *id.* at 927 (internal quotations omitted)(emphasis in origi-

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[3] That the prosecution histories of the '824 and '767 Patents reveal "A" moieties disclosing only biotin and iminobiotin, indirectly detectable moieties, does not necessarily compel a finding that the patents fail to meet the written description requirement with respect to direct detection, particularly given that the letter defendant sent to the U.S. Patent and Trademark Office ("PTO") protesting issuance of the '767 Patent could be interpreted as reflecting Applera's understanding that the '767 and '824 Patents cover direct detection. (See Letter from Applera's Senior Patent Counsel Stephen C. Macevicz to Assistant Commissioner of Patents Lawrence J. Goffney, Jr., Pls. Ex. 20, at GT008336 ("Nothing in any of the Ward specifications, the prosecution up to 1994, or pending claims up to 1994 give any indication that the invention includes compounds covering DNA sequencing fragments. . . . The only rationale for this claim is to obtain a claim that literally covers DNA sequencing fragments so that the opportunistic patent priorietor can extract royalties or other concessions out of the real industry participants under threats of patent infringement suits.").)

nal). The court found that the language of the specification had cast too wide a net, cautioning that while patent applicants need not provide a step-by-step narrative of reduction to practice, an ordinarily skilled artisan cannot be left with "a vague functional description" which does not fairly delineate the infringing from the non-infringing, *id.* at 926, 927. *See also Lizardtech, Inc. v. Regents of the Univ. of Cal.*, 424 F.3d 1336, 1346 (Fed.Cir.2005) (affirming judgment of invalidity where patent specification recited the procedure by which to manufacture one possible invention purported to be covered by the patent, but where specification was impermissibly vague as to the range of inventions covered thereby).

The facts at bar do not present the Court with such a clear want of specificity. While the text of the specification, which repeatedly discusses the "A" moiety as "forming a detectable complex with a polypeptide, suggests disclosure of only indirect detection, the record contains clashing but reasonable expert interpretations of the meaning of Example 9. Thus, the Court concludes that defendant has not proven by clear and convincing evidence that a skilled practitioner would read the '824 and '767 Patents to disclose *only* indirect detection, and summary judgment on this point is inappropriate.

B. *Enablement*

Next, defendants claim that Ward Patents '824 and '767 are invalid for lack of enablement under Patent Act § 112 ¶ 1, which requires the specification's language to include "such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the [invention]." Applera notes that in an unrelated interference proceeding before the U.S. Patent and Trademark Office ("PTO") on May 3, 2007, concerning a patent outside this case being disputed by Enzo and Applera,[4] Enzo's expert Dr. Bruce A. Roe submitted a declaration asserting that direct labeling was not enabled in any scientific publication until 1985. Since the Ward Patents were available before 1985, including European Patent No. 063879—the European equivalent of the Ward Patents, which was published on November 3, 1982, Ward Eur. Pat.App., Def. Supplem. Ex. 3,—Applera argues that Dr. Roe's opinion amounts to an admission by Enzo that the Ward patents do not enable the direct detection method, and that because the specification does not allow practice of the full scope of the claimed invention without undue experimentation, the Ward Patents are invalid for lack of enablement. Enzo accuses defendants of mischaracterizing Roe's testimony, which they claim pertained only to whether a specific labeling chemistry was actually disclosed in a particular patent, and point out that Roe admitted that he had not exhaustively searched the prior art before testifying.

The interference proceeding in which Roe's declaration was submitted was an *inter partes* PTO administrative proceeding to determine which of multiple entities first invented specific subject matter claimed in competing patents or patent applications. *See* 35 U.S.C. § 135. Claim 14 of the disputed '058 Patent, which is assigned to the California Institute of Technology and exclusively licensed to Applera, sets

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[4] Specifically, patent 5,821,058 ('058 patent), and allowed patent application 08/486,069.

out a method of DNA sequencing in which polynucleotide fragments are "tagged with a chromophore or fluorophore," that chromophore or fluorophore being a directly detectable label. (Roe Decl., Def. Supplem. Ex. 2, ¶ 21, quoting '058 Patent.) On May 3, 2007, Enzo moved that Caltech be denied the '058 patent's claimed "priority date" of January 16, 1984 on the grounds that the application on which Caltech bases its priority (No. 06/570,973 ("'973 Application")) lacks an enabled embodiment of Claim 14 of the '058 patent, because: "Methods for tagging nucleotides with fluorescent labels to determine the sequence of a polynucleotide were not publicly known until at least 1985." (Enzo Subst. Mot. in Interf. Procdg. 4, Def. Supplem. Ex. 1, at 4.)

In his declaration, Roe opines that a person skilled in the art, prior to 1985, "would not have been able to select the precise reagents, reaction conditions and process steps necessary to achieve a successful coupling of a chromophore or fluorophore from the multitude of possibilities, without at least undue experimentation." (Roe Decl., Def. Supplem. Ex. 2 ¶ 28.) In writing his declaration, Roe "reviewed the scientific literature published from about the late 1970s to about the late 1980s, in the field of DNA sequencing." (*Id.* ¶ 29.) At his deposition, Roe testified that his review of the literature before writing his report included "at least the Langer et al., that's David Ward I think is on that. I'd have to check." (June 12, 2007 Roe Dep., Def. Supplem. Ex. 4, at 116.)[5] When queried about the methods enabled by

[5] With respect to the Langer-Safer/Ward publication that Roe had reviewed (Langer-Safer (1981), see supra) on "enzymatic synthesis of biotin-labeled polynucleotides" (June 12, 2007 Roe Dep., Def. Supplem. Ex. 4, at 116-17), Enzo argues that Kricka's

the plaintiffs' '955 patent, Roe was unsure until given a chance to re-read the patent:

> Q: Let me be more specific, is there anything in this Ward patent that you could point me to that would tell a skilled person how to couple a fluorophore directly to a polynucleotide?
>
> A: Can I take some time to look through the patent?
>
> [. . . .]
>
> Q: Just to confirm, you've had the chance to look through the Ward '955 patent?
>
> A: Yes, I have.
>
> Q: And is there anything in that patent that would teach a person of skill how to directly couple a fluorophore to a polynucleotide? And let me just be clear, when I say directly, I mean by a covalent bond whether through a linker arm or not.
>
> A: No. Thank you for giving me time to look through that.

(*Id.* at 133.) Dr. Roe certified the accuracy of the deposition transcript, and did not submit any amendments or corrections.

The key inquiry is the extent to which the subject matter of Roe's testimony ("coupling a fluorophore or chromophore to the 5' amino of a polynucleotide fragment in a manner suitable for determining the

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knowledge of this article is irrelevant because it disclosed no example of direct labeling, in contrast to Examples 7, 8, and 9 of the Ward Patents specification. As the same arguments are made here regarding the Examples as in relation to the lack of written description, *supra*, the Court will not restate its analysis.

sequence of the polynucleotide" (Roe Decl., Pls. Supplem. Opp. Ex. 2, ¶ 26)) constitutes direct detection and hybridization. If the coupling testified to by Roe signifies direct detection and hybridization, then Roe's testimony can be taken to mean that detection and hybridization were not enabled before 1985.

In the Court's view, the question of the breadth of Roe's testimony is resolved by his clarification that his interference declaration merely states that "certain coupling chemistry was not known before a certain date" (*id.* at 26) (emphasis added), and that the declaration itself addresses the '973 Application and the "aliphatic amino group at the 5' terminus" (Roe Decl., Pls. Ex. 2, ¶¶ 25, 26, 30, 35, 38). A later declaration by Roe in the same proceeding confirms the conclusion that Roe's denial of enablement in the Ward patents is limited to a particular procedure not at issue in this litigation:

> All the steps for conducting DNA sequencing were known to a person of skill in the art in 1982 except for the step of tagging a polynucleotide fragment with a chromophore or fluorophore in a manner suitable for determining the polynucleotide sequence from the fragments in accordance with the Count.

(Roe Second Decl., Def. Supplem. Reply Ex. 1, ¶ 60.) Moreover, Enzo rightly points out that Applera's own expert Kricka testified and stated in his report on invalidity that direct labeling was known in the field by the time the first Ward patent issued in 1981 (Kricka Expert Report, Pls. Ex. 8, ¶ 30; Kricka Dep., Pls. Ex. 9, at 170), with which assessment Enzo's experts Sinden and Sherman agreed (Sinden Reply Expert Report, Pls. Ex. 7 ¶ 56; Sinden Dep., Pls. Ex.

6, at 46; Sherman Dep., Pls. Ex. 5, at 110). However, as Applera notes, the experts agreed that attachment of fluorescent labels for hybridization was known in 1981, not that the specific method suitable for DNA sequencing was known. (Def. Supplem. Reply at 8.)[6]

As the declaration of Roe is focused on what was known about direct detection in relation to 5' amino coupling in the '058 Patent/'093 Application context, the evidence proffered in support of defendant's enablement ground for invalidity does not compel granting summary judgment.

C. *Claim definiteness*

Applera argues that the Ward Patents are invalid because the term "interfering substantially" does not meet the definiteness requirement of Patent Act § 112 ¶ 2, which demands that patent claims "particularly point[ ] out and distinctly claim[ ] the subject matter which the applicant regards as his invention," 35 U.S.C. § 112 ¶ 2, as understood by one skilled in the art, *Invitrogen Corp. v. Biocrest Mfg.*, 424 F.3d 1374, 1383 (Fed.Cir.2005). The exact words employed in a patent specification are vital, as "claims delineate the scope of the invention using language that adequately notifies the public of the patentee's right to exclude." *Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1347 (Fed.Cir.2005). A claim will be rejected for indefiniteness where it "is not sufficiently precise to

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[6] Plaintiffs also point out that Applera's anticipation argument, see infra, is itself premised on the notion that direct labeling of nucleic acids was known before 1981. *See Elan Pharm., Inc. v. Mayo Found. for Med. Educ. & Research*, 346 F.3d 1051, 1054 (Fed.Cir.2003) (A patent claim "cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled.").

provide competitors with an accurate determination of the 'metes and bounds' of protection involved." *Ex parte Lyell*, 17 U.S.P.Q.2d 1548, 1550-51 (Bd. Pat.App. & Int.1990). A specification invites a determination of indefiniteness when it "leaves those skilled in the art entirely without guidance" as to the scope of requirement, *Exxon Research and Eng'g Co. v. United States*, 265 F.3d 1371, 1379 (Fed.Cir.2001), adrift without the "objective anchor" which makes a term definite, *Datamize*, 417 F.3d at 1350. Where, as here, the term in question expresses a measure of degree, "the district court must determine whether the patent's specification provides some standard for measuring that degree." *Seattle Box Co. v. Indus. Crating & Packing, Inc.*, 731 F.2d 818, 826 (Fed. Cir.1984). For understandable reasons of fundamental fairness to others practicing the art, the presence or absence of a standard "cannot depend solely on the unrestrained, subjective opinion of a particular individual purportedly practicing the invention." *Datamize*, 417 F.3d at 1350.

The terms "not interfering substantially" and "does not substantially interfere" appear in Claims 1, 42, and 48 of the '767 Patent; Claim 1 of the '824 Patent; and Claims 1 and 2 of the '928 Patent. In Claim 1 of the '824 patent, the term appears as follows: "said linkage group not interfering substantially with the characteristic ability of said compound to hybridize with said nucleic acid or of A to be detected." The Court's Claim Construction Ruling read this to mean that "the linkage group neither substantially interferes with the ability of the compound to hybridize with the nucleic acid nor substantially interferes with the ability of A to be detected." *Enzo Biochem*, 2006 U.S. Dist. LEXIS 74570 at 17.

Defendant contends that a person of skill in the art would not be able to determine from the specification how to measure "interference" in the context of "hybridization" and "detection."[7] Defendant also urges that the specification fails to provide guidance as to how to assess whether "interference" is present, since the significance of nucleotide alteration may vary according to the length of a polynucleotide (*i.e.*, the alteration of a single nucleotide would affect hybridization more profoundly on a shorter chain than on a longer one).

For its part, Enzo argues that this Court construed the term during the claim construction phase, and is therefore prevented from finding the term indefinite, citing two recent decisions from the Federal Circuit, *Energizer Holdings, Inc. v. Int'l Trade Comm'n*, 435 F.3d 1366, 1371 (Fed.Cir.2006) (noting that "[a] claim that is amenable to construction is not invalid on the ground of indefiniteness") and *Aero Prods. Int'l, Inc. v. Intex Recreation Corp.*, 466 F.3d 1000, 1016 (Fed.Cir.2006) (stating the corollary, that "if a claim is not amenable to construction, the claim is invalid as indefinite under 35 U.S.C. § 112, ¶ 2").

However, in both *Aero Products* and *Energizer*, the trial court had assigned precise definitions to the terms at issue during the claim construction phase.

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[7] Plaintiffs emphasize that words of degree like "substantially" are not *per se* indefinite, *see, e.g., Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1575-76 (Fed.Cir.1986) ("so dimensioned"); *BJ Servs. Co. v. Halliburton Energy Servs., Inc.*, 338 F.3d 1368, 1372-73 (Fed.Cir.2003) ("about"), but this contention misses the mark of Applera's argument, which is specific to whether the claims at issue sufficiently define the meaning of "not interfering substantially" and "does not substantially interfere."

In *Energizer*, the dispute centered on the phrase "said zinc anode," and the narrow question of whether the phrase properly referred to a specific antecedent term, 435 F.3d at 1368-1369. In *Aero Products*, the Federal Circuit weighed the definiteness of the phrase "complete hermetic seal," which the trial court had construed as meaning "a seal that does not require any additional parts to retain nearly or largely all of the air in the bed," 466 F.3d at 1008. The district court struck this compromise between two very specific construction proposals—the plaintiff's "seal that does not require any additional parts to retain 'nearly' or 'largely' all of the air in the bed such that the bed maintains its desired firmness for the expected duration of use," and the defendant's terser "nearly or largely impervious to air," *id.*

Here, the parties have presented this Court not with specificity, but with an adverbial phrase which, when added by the plaintiff as an amendment to the original patent in 1986,[8] was presumably meant to distinguish the Ward method of detection and hybridization from other methods which did cause substantial interference. At construction, neither party proposed a concrete definition for "substantial interference" expressed in signal-to-noise ratios, temperature, time, or any other laboratory metric which a practitioner could use as a milepost when performing hybridization and detection. Enzo proposed that the term be taken to mean, recursively, "not rendering impractical or overly difficult," Pl.'s Cl. Constr. Memo [Doc. # 89] at 23. Applera,

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[8] Supplemental Amendment application dated Mar. 21, 1986 reproduced at defendant's memo in support of summary judgment on invalidity [Doc. # 185], Ex. 23.

meanwhile, proposed that the term be read as effectively meaning that the binding procedure function transparently, such that:

> that the ability of A (when attached to B via said linkage group) to form a detectable complex is essentially identical to the ability of A to form a detectable complex when directly attached to B.

Def.'s Cl. Constr. Memo [Doc. # 91-2] at 22-23. Beyond that, the parties' arguments on both construction and definiteness of the key phrase has been comparatively sparse, with defendants reserving argument on construction of "substantial interference" in the interest of arguing for indefiniteness at summary judgment,[9] and plaintiffs' reply construction brief not even listing "substantial interference" as an area of dispute.[10] Faced with the parties' two alternative meanings of "substantial interference," this Court chose to use the term to limn the behavior of the linkage group, but could not affix a more precise technical definition.[11]

Defendant's expert Kricka states in his report that "[t]he term 'not interfering substantially' in the context of 'hybridization' and/or 'detection' does not appear anywhere in the specification outside of the claims," and thus "provides no guidance to allow one skilled in the art to measure 'interference' in the

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[9] Defs.' Cl. Constr. Br. at 22.

[10] *See* Pl. Reply Cl. Constr. Br. [Doc. # 98] at i.

[11] The Court ruled that "substantial interference" will be taken as meaning that "the linkage group neither substantially interferes with the ability of the compound to hybridize with the nucleic acid nor substantially interferes with the ability of [the A moiety] to be detected. *Enzo Biochem, Inc. v. Applera, Inc.*, 2006 U.S. Dist. LEXIS 74570 at 16.

context of 'hybridization' and 'detection.'" (Kricka Decl. ¶ 129.) Kricka further states that "there is no guidance in the specification for one to determine how to assess if there was any 'interference'" at all, given that "[w]hile a very minor alteration of a single nucleotide in a chain of three nucleotides would have a profound effect on the ability of that oligonucleotide to hybridize, the same modification on a longer oligonucleotide, such as one having 50 or 100 nucleotides, might not have any effect on hybridization." (*Id.* ¶ 130.) Defendant notes that Enzo's Vice President Dr. Dean Engelhardt testified that he did not know how one should measure the attribute of not substantially interfering. (Jan. 16, 2007 Engelhardt Dep., Def. Ex 25, at 128-29.) Similarly, Enzo's Vice President of Clinical Affairs, Dr. Barbara Thalenfeld, when asked how she would "measure whether only the linkage group does or does not interfere with hybridization" or "if the linkage group itself was interfering with the ability of the reporter to be detected," responded "I don't know." (Thalenfeld Dep., Def. Reply Ex. 6, at 178-79.)

The plaintiffs, relying upon the opinion of expert Sinden, argue that the term is sufficiently definite. Sinden opined that "substantial interference" is "clear and plain language" which denotes the point at which [something] will "prevent you from getting the experiment to work." (Apr. 13, 2006 Sinden Dep., Pls. Opp. Ex. 11, at 138:11-15). Sinden's report observes that the term means that "the linkage group may interfere with hybridization and detection so long as the interference is not substantial, *i.e.*, an amount that would render hybridization or detection impractical or overly difficult." (Sinden Report, Pls. Ex. 17, at 29). He also explained at his deposition how

temperature affects DNA hybridization and that a linker arm that altered the melting temperature of particular DNA would bear on "substantial interference." (Apr. 13, 2006 Sinden Dep., Pls. Opp. Ex. 11, at 134-36.)[12]

While arguing that the approach of the point of failure ("impractical or overly difficult"), is measurable in terms of "degrees of interference" (Apr. 13, 2006 Sinden Dep., Pls. Opp. Ex. 11, at 139:2-3), when pressed to identify the precise point at which interference ripens to substantiality, Sinden stated:

> It's probably in the hands of the experimenter. Clearly, if it didn't work at all, it wouldn't work. If it worked 50 percent and you were able to get your signal and publish a paper, you may go with it.

(*Id.* at 139:8-12.) Moreover, Sinden concedes that inasmuch as his report equates substantial interference with the point at which hybridization or detection becomes overly difficult, "[o]verly difficult may mean different things to different people." (Apr. 13, 2006 Sinden Dep., Def. Ex. 9, at 139-40.) Sinden's testimony would thus seem to corroborate Kricka's view that the face of the patent's specification provides no standalone gauge of "substantial interference," but rather requires experimentation in

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[12] For his part, Kricka admits that "melting temperature of modified polynucleotides could conceivably be one measure of the effect of a linker arm on hybridization." (Kricka Decl. ¶ 129, citing Claim Construction Ruling at *16.) Even though Kricka and Sinden agree that melting temperature could have an effect on hybridization, plaintiffs have not pointed to anything in the patents instructing a person of skill in the art on how to determine substantiality of interference based upon melting temperature of polynucleotides.

order to determine where the claims set forth in the Patents become useful. Left to Sinden's interpretation, the Patent claims would cover any interactions which succeed, but not those which do not—rendering "substantial" a nullity. Moreover, it is instructive that neither Thalenfeld nor Engelhardt, both scientists and Enzo executives, could conjecture a means of determining substantiality of interference.

As this Court understands that allegations of indefiniteness may not be rebutted merely by the unrestrained, subjective opinion of the inventor, the claims must fail. In *Datamize*, the Federal Circuit affirmed a finding of indefiniteness where a patent specification purported to cover the creation of "aesthetically pleasing" elements in a computer graphical user interface. The deficiency in such a term, the Court found, was that Datamize had "offered no objective definition identifying a standard for determining when an interface screen is 'aesthetically pleasing,'" *Datamize*, 417 F.3d at 1342, but instead simply provided the testimony of an expert who listed elements of design which would lead one skilled in the art to deem a given user interface "aesthetically pleasing." The Court found that an expert's list of elements or indices alone "fails to explain how the parameters should be evaluated or weighed to reach the conclusion" that a given creation meets the patent's subjective standard. *Id.* at 1354, *see also Honeywell Int'l, Inc. v. Int'l Trade Comm'n*, 341 F.3d 1332, 1339 (Fed.Cir.2003) (affirming judgment of invalidity where the proper temperature at which a crucial step in the manufacturing-process invention was to take place was provided only by the testimony of patent holder's expert).

The Federal Circuit's treatment of indefiniteness in *Exxon* also informs this Court's decision. The two patents at issue in that case covered "improvements in what is known as the Fischer-Tropsch process for converting natural gas to liquid hydrocarbon products," *Exxon*, 265 F.3d at 1373, which, if implemented, would "increase[ ] the relative catalyst productivity in the Fischer-Tropsch reaction by at least 30%" and "optimally operat[e] a slurry bubble column . . . to produce hydrocarbon products at an increased rate." *Id.* at 1374. While the trial court had determined that four of Exxon's claims were indefinite for indefiniteness, the Federal Circuit reversed. Three of those claims centered on numerical terms,[13] but the analysis of most interest here is the Federal Circuit's treatment of a term which was not expressed within a mathematical formula, "substantial absence of slug flow."[14] In the district court, defendants had argued that gauging the substantiality of slug flow was not possible given that the specification did not set forth the proper means by which slug flow was to be measured. The Federal Circuit found the term to be sufficiently definite when read within the context of the entire patent, i.e. a system by which to increase efficiency of the Fischer-Topsch reaction by at least

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[13] *See Exxon Research and Eng'g*, 265 F.3d at 1377 (deeming "to increase substantially" sufficiently definite where patent specification defines such an increase in catalyst activity as being between between 30-75%), *id.* at 1378 (holding "for a period sufficient" to be definite where the patent specification set out a minimum time period for sufficiency, but not a maximum time), *id.* at 1382 (finding that specification that particles be of an "average diameter" set forth in a mathematical formula acceptably definite).

[14] Apparently referring to the movement of large gas bubbles through the reactor.

30%. Because the patent specification taught that slug flow interferes with the efficient completion of the patented method, the Court held that the substantial absence of slug flow "can be determined with reference to whether reactor efficiency is materially affected," as measured by identifiable data points such as mass transfer performance. *Exxon*, 265 F.3d 1380-1381. Thus, by measuring the efficiency of their reactions—the innovation claimed by Exxon—practitioners could determine whether or not a particular procedure infringed upon Exxon's patent.

By contrast, the Ward patents do not set forth improvements upon a known process, but rather, describe a new procedure of non-radioactive detection and hybridization which does not cause "substantial interference" with a successful result. The specifications neither set forth how one would gauge substantial interference, nor delimit the threshold at which interference with the procedure prevents Ward's method from being implemented. As plaintiff's expert Sinden frankly admitted, substantial interference has thus been left to the experimenter to determine the conditions under which detection and hybridization either succeeds or fails. Although the patent expresses a term of degree ("substantial interference"), expert testimony has shown the term to be an illusory yardstick which, if permitted to stand, would sweep all successful hybridization and detection into the ambit of the patents' coverage, while excluding any unsuccessful procedures. This effect would be entirely unlike Exxon's patents, which covered only those Fischer-Tropsch reactions which were made observably more efficient by use of the patented methods. It cannot be the case that a term added as a limiting clarification to the Ward

patents can now be used to amplify the patents' coverage.

In sum, plaintiff has been caught in one of patent law's traps: having used language in its patent application which stakes out the zone of exclusivity for its invention, the plaintiff must now be able to show that its language is nonetheless definite enough to put others skilled in the art on notice of what has been patented. Because defendant has proven by clear and convincing evidence that the term "interfering substantially" in Claim 1 of the '824 Patent; Claims 1, 42, and 48 of the '767 Patent; and Claims 1 and 2 of the '928 Patent is indefinite, summary judgment of invalidity for indefiniteness is granted on these patent claims.

D. *Anticipation*

Although the indefiniteness of the claims at issue is fatal, thoroughness counsels addressing all of the parties' remaining arguments. As a third ground of invalidity, defendant asserts that the '824, '767, and '928 patents were anticipated by three prior art references published before April 17, 1981 (the date that the original Ward patent application was filed): a journal article by Alfred Pingoud, *et al.* published in 1977; a journal article by Hiroshi Kasai, *et al.* published in 1979; and a doctoral thesis by J.G.J. Bauman published in 1980. (*See* Alfred Pingoud, *et al.*, "Fluoresceinylthiocarbamyl-tRNA: a useful Derivative of tRNA (E.coli) for Physiochemical Studies," *Nucleic Acids Res.* (1977) ("Pingoud"), Def. Ex. 27; Hiroshi Kasai, *et al.*, "Specific Fluorescent Labeling of 7-(aminomethyl)-7-deazaguanosine Located in the Anticodon of tRNA Isolated from E. Coli Mutant," *Nucleic Acids Res.* (1979) ("Kasai"), Def. Ex. 28;

J.G.J. Bauman, "Cytochemical Detection of Specific Nucleic Acid Sequences Development and Application of In Situ Hybridisation Methods for Fluorescence Microscopy" (doctoral dissertation) (1980) ("Bauman"), Def. Ex. 29.) Specifically, Applera contends that Kasai anticipates the '767 and '824 Patents; Pingoud anticipates the '767 and '928 Patents; and Bauman anticipates all three patents. Plaintiffs argue that none of the three publications discloses every claim asserted as construed by the Court and that a genuine issue of material fact exists as to whether the articles are enabling references that qualify as "prior art."[15]

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[15] The Court disposes briefly of Sherman's general attack on the three references for failing to meet "the standard that an organic chemist in the early 1980's would have used in order to determine whether or not a new organic molecule had been synthesized" and as thus being non-enabling (Sherman Decl. ¶ 33). Without citation to any authority, Sherman conclusorily states that a publication "lacking a sufficient number of [10] criteria" would not be considered to provide necessary disclosure to enable one of skill in the art to make and use a new chemical substance, and thus that Kasai and Pingoud in particular should be rejected as prior-art references because they are not enabling. (*Id.*) Sherman's proffered rubric, however, is unsubstantiated and thus rejected as a general argument against defendant's anticipation claims. Moreover, as defendant points out, Kasai and Pingoud were in any case published in the journal Nucleic Acids Research; and for a reference to be enabling, "all that need be shown is that one of skill in the art could make the disclosed compounds," not that it was actually made. (Def. Reply Mem. at 7-8, citing *In re Donohue*, 766 F.2d 531, 533 (Fed.Cir.1985) ("[E]ven if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling. . . . It is not, however, necessary that an invention disclosed in a publication shall have actually been made in order to satisfy the enablement requirement.").) *See Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d

Whether a patent claim is anticipated under 35 U.S.C. § 102 is a question of fact requiring element-by-element evaluation of the disclosure of the claims in the prior art reference, as "each and every limitation . . . either expressly or inherently" must be disclosed, *Bristol-Myers Squibb Co. v. Ben Venue Labs. Inc.*, 246 F.3d 1368, 1374 (Fed.Cir.2001). "A claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." *Elan Pharms., Inc.*, 346 F.3d at 1054 (internal quotation marks and citation omitted).

1. *Kasai*

Kasai "describes a procedure for fluorescent labeling of E. coli preQ1-containing $tRNA^{Tyr}$ with dansyl chloride." (Kasai, Def. Ex. 28, at 232.) The article reports that "[t]he modified $tRNA^{Tyr}$ was found to be active both in amino-acylation and in binding to ribosomes" and that "this fluorescent probe should be useful for conformational studies on tRNA." (*Id.*) Defendant argues that Kasai discloses a labeled polynucleotide sequence (dansyl-tRNA) that meets each limitation of the relevant claims of the '767 and '824 Patents.

a. *'767 Patent*

To illustrate what it alleges to be the anticipation of the '767 patent, Applera focuses on the sugar moiety-containing oligo-/polynucleotide of Claim 48, arguing that Kasai's tRNA compound includes

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1368 (affirming partial denial of summary judgment of invalidity for anticipation where anticipatory experiment "enabled the performance of [antitumor drug administration] steps even though [it] did not achieve a favorable outcome").

-CH2-NH-, the aminomethyl linkage group whose structure is "preferred" in the Ward Patents specification, which constitutes Claim 8 of the '767 Patent and Claim 16 of the '928 Patent. Defendant claims that Kasai's tRNA compound hybridizes with complementary polynucleotides and becomes detectable via measurement of the fluorescence of the dansyl moiety, Kasai Fig. 2, Def. Ex. 28, at 235—thus, because hybridization and detection are made possible in this fashion, that Kasai meets the "not substantially interfere" limitation. Although this Court has determined that the "substantially interfere" language in the Ward Patents is the basis for their invalidity, interpretation of the phrase for purposes of anticipation does not affect the invalidity ruling.

Enzo's expert Sherman disputes the satisfaction of the "not substantially interfere" limitation by stating that the aminomethyl group serving as a linker arm in the compound "would not provide sufficient rigidity to prevent significant interference with hybridization of a complementary polynucleotide. Indeed, one would predict based on the flexibility of this functional group and the concomitant high degree of motion, there would be significant interference due to free rotation about the single bonds." (Sherman Decl. ¶ 44.) However, as defendant notes, Sherman offers no support, experimental, literary, or otherwise, for this assertion. In addition, implicit in Sherman's observation about the aminomethyl-group linker is a definition of substantial or significant interference as allowing for hybridization, which conflicts with Sinden's interpretation of the term "not substantially interfere" as "it can't prevent you from getting the experiment to work." See Apr. 13, 2006 Sinden Dep., Def. Ex. 9, at 138.

A general retort made by plaintiffs is that Kasai cannot be anticipatory because it is directed to naturally substituted bases, *viz.* preQ1, which Enzo contends is "specifically excluded from the Ward Patent claims." (Sherman Decl. ¶ 42.) Enzo cites the specification, which reads that "7-deazapurines useful in this invention must not be naturally substituted at the 5- or 7-positions, respectively." ('824 Patent at 7:64-67.) Defendant responds that Sherman relies on the specification rather than the patent claims, impermissibly importing limitations into the claims for purposes of avoiding prior art. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1323 (Fed.Cir.2005). Moreover, Applera claims that the phrase from the specification is quoted out of context and in fact "refers to the fact that the Ward patents' described methods for adding linkage groups to the 5-position of pyrimidines and the 7-position of 7-deazapurines will not work if there is already a carbon-carbon bonded substituent at these positions such as in thymine, 5-methylcytosine, and 5-hydroxymethylcytosine," *i.e.*, that "modified bases derived from bases lacking natural substitutions at the 5- or 7-positions 'are more readily prepared or used or both, and therefore are presently preferred.'" (Kricka Reply Decl. ¶ 8, citing '824 Patent at 7:53-57.) Kricka opines that "Kasai discloses how to synthesize 7-(aminomethyl)-7-deazaguanosine and react this compound with dansyl chloride. . . . Therefore, one of skill in the art could make an 'unnaturally' substituted 7-deazapurine and label it with a fluorescent dye if they wished." (*Id.* ¶ 11.) The Court agrees that the Ward Patent claims do not contain a specific limitation which excludes all naturally-occurring linkage groups (modified 7-deazapurine bases), and

thus, a finding that Kasai anticipates the '767 Patent is not precluded. Defendant has met its burden of proving Kasai's anticipation of each limitation of every asserted claim of the '767 Patent.

b. *'824 Patent*

The arguments with respect to Kasai's alleged anticipation of the '824 Patent, including the non-naturally occurring argument, are basically identical to those above for the '767 Patent. The '824-specific arguments are addressed here.

Kasai discloses that "binding of danyslated Tyr-tRNA$^{Tyr}_{preQ1}$ to E. coli ribosomes was stimulated by template, poly(U, A, C)." (Kasai, Def. Ex. 28, at 236.) According to Kricka this anticipates Claim 1's method for detecting nucleic acids (poly(U, A, C) or poly(U, C) containing ribosomal RNA) that hybridize or bind with the dansyl-labeled polynucleotide tRNA^{Tyr}. (Kricka Decl. ¶ 68-76; Kasai, Def. Ex. 28, at 236-38.) Sherman disputes this by asserting that the tRNA in Kasai is used for "conformational characterization," not detection of nucleic acids, and does not disclose hybridization between two complementary polynucleotides, but between a polynucleotide and a stimulated ribosome. (Sherman Decl. ¶¶ 51-53.) However, Kricka explains that the ribosomal RNA of E. coli used in Kasai is referenced as a type of polynucleotide in the '824 Patent ('824 Patent at 17:24), and thus that when the "tRNA binds to a ribosome, portions of the tRNA hybridize to portions of the ribosomal RNA at various stages in the translation process. At the same time, the anticodon portion of the tRNA hybridizes with codon portions of another polynucleotide" (Kricka Reply Decl. ¶ 29). Indeed, Kasai notes that "[b]inding of [^{14}C]Tyr-tRNA to E. coli ribosomes in the presence of polynucleotide

template was carried out as reported by Nishimura *et al.*" (Kasai, Def. Ex. 28, at 233), indicating that tRNA-ribosome bonding was an established form of polynucleotide hybridization. As plaintiffs fail to rebut defendant's proof of anticipation, and for the reasons stated above with respect to the '767 Patent, the Court finds that defendant has proven by clear and convincing evidence that Kasai anticipates every claim of the '824 Patent.

2. *Pingoud*

Pingoud describes the labeling at "uncommon base Q"—which had recently been identified when Pingoud was published and was later supplanted in Kasai by the preQ1 nucleoside—of the modified tRNA polynucleotide "FTC-$tRNA^{Tyr}$," and shows to what extent the modification affects the biological activity of the tRNA. (Pingoud, Def.Ex.27.) Applera contends that Pingoud is an anticipatory reference as to the '767 and '928 Patents.

a. *'767 Patent*

Defendant contends that Pingoud discloses the labeled polynucleotide FTC-$(QU)_n$, whose structure is described in the claims of the '767 patent. The structural identity of the nucleotides is substantially undisputed, except that plaintiffs again make the same argument as with Kasai that apropos the linkage group, the "does not substantially interfere" limitation is unmet, and that the "naturally substituted" limitation is implicit in the claim—the same arguments made with respect to anticipation based on Kasai. For the same reasons these arguments were rejected *supra*, the Court rejects them here, and the Court has in any case concluded that Patent '767 is invalid for anticipation by Kasai.

b. *'928 Patent*

Kricka opines that Claims 1 and 2 of the '928 patent were disclosed by Pingoud. As to Claim 1, Applera reads Pingoud as disclosing a fluorescein labeled 7-deazaguanosine nucleoside that is "[a] compound useful as a probe for detecting the presence or absence of a nucleic acid" to either detect the presence of $tRNA^{Tyr}$ when the nucleoside is incorporated into the polynucleotide, or by digesting the polynucleotides to individual nucleosides and then detecting the disclosed labeled nucleoside. As to Claim 2, defendant makes the same arguments for the terms of that claim which are identical to that of Claim 1 and adds that the labeled polynucleotide $FTC\text{-}(QU)_p$ is useful as a probe to detect $tRNA^{Tyr}$.

The locus of debate with respect to the '928 Patent concerns the "A" moiety in Claims 1 and 2, which "represents at least three carbon and an indicator molecule," and intersects with the question of whether both indirect and direct detection are disclosed by the Patent. As the Court determined *supra* that Applera has failed to meet its burden of proving invalidity for lack of written description as to direct detection, the Court evaluates whether Pingoud is anticipatory as to both indirect and direct detection. The parties agree that in order to have anticipated the '928 Patent, Pingoud's "A" moiety must consist of a fluorescein dye indicator molecule and another portion containing at least three carbon atoms. Defendant argues that "the fluoresceinyl-thiocarbamyl moiety [in Pingoud] is split into two components: a portion of the fluorescein dye that can independently act as a fluorescent dye and another portion containing at least three carbons." (Def. Mem. at 39.) Enzo contests that the moiety can really be

"split," and points to Kricka's testimony "that one of skill in the art would not consider breaking up fluorescent molecules into their constituents." (Kricka Reply Decl. ¶ 33; Kricka Decl. in Supp. of Def. Mot. for Summ. J. of Non-Infr., Pls. Ex. 25 ¶¶ 30, 31.) Although Kricka defends his comment as responsive to Sinden's "advocat [ing] breaking single fluorescent dyes into constituent parts" (*id.*), Sinden's testimony was directed to splitting a compound consisting of a fluorescein donor dye attached to a rhodamine acceptor dye, *i.e.*, the structure of defendant's allegedly infringing compounds. (Sinden Decl. in Supp. of Pls.' Opp. to Def. Mot. of Summ. J. of Non-Infr., Pls. Ex. 24, ¶¶ 29-31.)

As the party claiming invalidity, defendant's burden is high: Applera must prove invalidity by "clear and convincing evidence as to underlying facts," *Rockwell Int'l Corp.*, 147 F.3d at 1364. Here, the combination of Kricka's disavowal that one would split fluorescent dyes like that in the Pingoud moiety, taken together with defendant's failure to show that Sinden's discussion of splitting applied outside the context of Applera's fluorescein-rhodamine compound, prevents this Court from concluding that Pingoud's moiety meets the three-carbon-plus-indicator-molecule limitation in the '928 Patent, and thus defendant's Motion of invalidity for anticipation based on Pingoud is denied with respect to '928 Patent Claims 1 and 2.

3. *Bauman*

The third article claimed to be prior art is a doctoral thesis written by Dutch scientist J.G.J. Bauman, which was publicly available more than one year

prior to the filing of the original Ward patent.[16] Chapter 8 of Bauman's thesis sets forth a method of indirect detection involving the incorporation of pyrimidine nucleotides labeled with a Hg-Glutathione-Trinitrophenyl ("TNP") hapten and fluorescent antibodies to TNP. Defendant claims that Bauman shows that the hapten-labeled polynucleotide can be used as a probe in a hybridization assay to detect the presence of nucleic acids in a sample, and is thus an anticipatory reference of the three Ward Patents.[17]

The parties make generalized arguments not specific to the particular claims. First, the parties dispute whether the mercury-glutathione linker (the mercury bonds are the C-Hg bond between A and B and the Hg-S bonds in A) in Bauman is usable for typical hybridization experiments. Bauman explains that under certain conditions there were "[p]roblems observed in hybridising mercurated polynucleotides." (Bauman, Def. Ex. 29, at 161.) However, it notes that "[t]he loss of mercury during the hybridisation as a result of the thermal instability of the -C-Hg-bond (Dale and Ward, 1975) can be avoided by using low tempoeratures and formamide containing buffers." (*Id.* at 162.) According to Applera, this remedial prescription makes the Bauman compound usable in hybridization, and plaintiffs offer no evidence to

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[16] Enzo's concern about the non-disclosure of the full Bauman reference was cured by submission of the entire dissertation and accompanying documents with Applera's reply memorandum.

[17] Sherman argues that Claim 21 of the '824 Patent and Claim 70 of the '767 Patent should not be deemed asserted as anticipated by Bauman because they are not specifically addressed in Kricka's chart illustrating the anticipation claimed. (Sherman Decl. ¶¶ 66, 67.) However, these claims are in fact addressed in that chart. (*See* Kricka Decl.App. A. at 18, 32.)

rebut this, except to cite one sentence of the Ward Patents specification,[18] Sherman Decl. ¶ 72. However, this section of the specification does not address mercury, and Sherman does not explain how this bears on the analysis. Thus, the inaptness of mercuriated polynucleotides for hybridization does not dispose of the anticipation argument.

Second, Enzo and Applera disagree as to whether the mercury ligand in Bauman substantially interferes with hybridization. The indirect detection method in Bauman begins with RNA "mercurated by incubation in mercuric acetate," but at the next step, "[t]he acetate ligand of the mercuri-nucleotides is replaced by the CN ion, in order to facilitate hybridisation." (Bauman, Def. Ex. 29, at 142-43.) That this alteration is required, plaintiffs argue, signifies that "the glutathione linkage group interferes with hybridization" (Sherman Decl. ¶ 74). Moreover, Enzo points out that Bauman uses the synthetic homopolymer poly(U) in its experiments, which plaintiffs claim "provides an increased incidence of hybridization allowing for a greater amount of interference to occur without resulting in failure of hybridization," Sherman Decl. ¶ 76. However, in addition to Sherman's failure to support his statement that use of Poly(U) results in increased hybridization and thus greater interference, Applera correctly points out that the Ward Patents do not preclude use of unnatural homopolymers; in fact, the specification itself states, "Another embodiment of

[18] '824 Patent at 6:64-68 reads: "[T]he physical and biochemical properties of polynucleotides containing small numbers of probe substituents should not be significantly altered so that current procedures using radioactive hybridization probes need not be extensively modified."

this invention involves detection of poly A-containing sequences using poly U" ('824 Patent at 24: 51-54). Thus, the Bauman references satisfy the "not substantially interfering" limitation in the Ward Patents.

The third aspect bearing on whether Bauman is anticipatory stems from the Court's construction of the Ward Patents as disclosing both direct and indirect detection. The claim language "wherein the moiety A comprises an indicator molecule" and "wherein A comprises an indicator molecule" from the '767 and '824 Patents, was interpreted in the Court's Claim Construction Ruling interpreted to mean "that A may be a part of or the entire signaling moiety." *Enzo*, 2006 U.S. Dist. LEXIS at 11-12. In no uncertain terms, the Court concluded at claim construction that "the plain language and structure of the '824 and '767 Patents indicate that these patents cover both direct and indirect detection." *Id.* at 9. While the parties agree that Bauman does not address direct detection, Applera argues that it need not include both direct and indirect detection to be anticipatory. However, the caselaw is clear that in order for a reference to be anticipatory, it must "disclose every limitation of the claimed invention, either explicitly or inherently," *Liebel-Flarsheim Co.*, 481 F.3d at 1381, and as Bauman only discloses indirect detection, it is not an anticipatory reference rendering Patents '767 and '824 invalid. Summary judgment of invalidity for anticipation is thus denied based on Bauman as regards the '767 and '824 Patents.

Lastly, with respect to the '928 Patent, in addition to the earlier discussion of whether B meets the "not substantially interfering" limitation, plaintiffs' expert Sherman applies the same reasoning discussed above

with respect to non-disclosure of direct detection to argue against anticipation. However, as diagrammed in defense expert Kricka's comparative chart, the three-carbon-plus-indicator-molecule structure is supported by the compound set out in Bauman: the complex consisting of the Hg-Glutathione-TNP, the rabbit TNP-antibody, and the swine antibody to the rabbit antibody. Kricka Decl.App. A at 83-84. As the other limitations are also diagrammed and well supported by defendant's expert, plaintiffs' brief retort is insufficient to rebut the evidence presented that '928 Patent Claims 1 and 2 are anticipated by Bauman. Summary judgment is granted on grounds of anticipation with respect to the '928 Patent.

III. *Conclusion*

Accordingly, the Court concludes that the Claims 1, 2, 8, 11, 13, 42, 46, 47, 48, 49, 50, 51, 67, 68, 70 of the '767 Patent; Claims 1, 18, 19, 21, 26, 28, 32, 33 of the '824 Patent; and Claims 1 and 2 of the '928 Patent are invalid based on anticipation by prior art. Defendant Applera's Motion for Summary Judgment of Invalidity [Doc. # 181] is therefore granted. The Clerk is directed to close this case.

IT IS SO ORDERED.

APPENDIX C

UNITED STATES COURT OF APPEALS
FEDERAL CIRCUIT

No. 2009-1281

ENZO BIOCHEM, INC., ENZO LIFE SCIENCES, INC., AND YALE UNIVERSITY,
Plaintiffs-Appellants,

v.

APPLERA CORP. AND TROPIX, INC.,
Defendants-Appellees.

May 26, 2010

Before MICHEL, *Chief Judge*, NEWMAN, MAYER, PLAGER,* LOURIE, RADER, BRYSON, GAJARSA, LINN, DYK, PROST, and MOORE, *Circuit Judges*.

PLAGER, *Circuit Judge*, dissents from the denial of the petition for panel rehearing.

ORDER

PER CURIAM.

Defendants-Appellees Applera Corp. and Tropix, Inc. filed a combined petition for panel rehearing and rehearing en banc. The panel requested a response from Plaintiffs-Appellants Enzo Biochem, Inc., Enzo Life Sciences, Inc., and Yale University. The court

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* Judge Plager participated only in the decision on the petition for panel rehearing.

granted Defendants-Appellees leave to file a reply. The petition for rehearing was considered by the panel that heard the appeal, and thereafter the petition for rehearing en banc, the response to the petition, and reply were referred to the circuit judges who are in regular active service.

Upon consideration thereof,

IT IS ORDERED THAT:

(1) The petition of Defendants-Appellees for panel rehearing is denied.

(2) The petition of Defendants-Appellees for rehearing en banc is denied.

(3) The mandate of the court will issue on June 2, 2010.

ON PETITION FOR PANEL REHEARING

PLAGER, *Circuit Judge*, dissenting from the denial of the petition for panel rehearing.

I respectfully dissent from the denial of the petition for panel rehearing on the question of indefiniteness. Despite the varying formulations that this court has used over the years in describing its "indefiniteness" jurisprudence to which the petitioner in this case points, the general conclusion from our law seems to be this: if a person of ordinary skill in the art can come up with a plausible meaning for a disputed claim term in a patent, that term, and therefore the claim, is not indefinite.[1] At least not so indefinite as

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[1] *See, e.g., Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1347 (Fed.Cir.2005) ("Only claims 'not amenable to construction' or 'insolubly ambiguous' are indefinite." (citing *Novo Indus., L.P. v. Micro Molds Corp.*, 350 F.3d 1348, 1353 (Fed. Cir.2003); *Honeywell Int'l, Inc. v. Int'l Trade Comm'n*, 341 F.3d

to run afoul of the statutory requirement that claims shall "particularly point[ ] out and distinctly claim[ ] the subject matter which the applicant regards as his invention." 35 U.S.C. § 112, second paragraph.

The corollary derived from this understanding is that if several persons of ordinary skill come up with competing but plausible interpretations of a disputed term—as is typically the case with competing "expert witnesses" in patent infringement litigation—the problem is not one of an inherently ambiguous and potentially indefinite claim term, but rather the problem becomes simply one of picking the "right" interpretation for that term.[2] Since picking the "right" interpretation—claim construction—is a matter of law over which this court rules, and since the view of the trial judge hearing the case is given little weight, so that the trial judge's view on appeal becomes just a part of the cacophony before this court, it is not until three court of appeals judges randomly selected for that purpose pick the "right" interpretation that the public, not to mention the patentee and its competitors, know what the patent

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1332, 1338 (Fed.Cir.2003); *Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed.Cir.2001))).

[2] Broad, to the point of inherently ambiguous, claim drafting is not just a matter of poor drafting skills on the part of some lawyers who prosecute patent applications. On the contrary, the art of broad claim drafting is a prized talent—clients are openly urged to use "broad patent protection both offensively to block competitors from the marketplace, and defensively to serve as a bargaining chip against potential patent infringement suits" and to "file patents to cover all aspects of the core technology . . . to create a 'picket fence' of protection." David J. Dykeman and Joanna T. Brougher, *File, Protect, Update, Defend*, Corporate Counsel, May 1, 2010, http://www.law.com/jsp/cc/PubArticleCC.jsp?id=1202447671049.

actually claims. The inefficiencies of this system, and its potential inequities, are well known in the trade.

The United States Patent and Trademark Office ("PTO"), by contrast, appears to be taking steps to give the statutory requirement real meaning. In 2008, the patent examining corps was given a five-page instruction on "Indefiniteness rejections under 35 U.S.C. § 112, second paragraph."[3] The memo initially observes that "[t]he primary purpose of the definiteness requirement for claim language is to ensure that the scope of the claims is clear so that the public is informed of the boundaries of what constitutes infringement of the patent."[4] The memo reviews in detail a recent opinion of this court, following which the memo states the position of the PTO: "If the language of a claim, considered as a whole in light of the specification and given its broadest reasonable interpretation, is such that a person of ordinary skill in the relevant art would read it with more than one reasonable interpretation then a rejection of the claim under 35 U.S.C. § 112, second paragraph, is appropriate."[5]

This memo was followed later in the year by a rare precedential opinion issued by the Board of Patent Appeals and Interferences ("Board") in *Ex parte Miyazaki*.[6] The Board noted that this court has in

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[3] Memorandum from John Love, Deputy Commissioner for Patent Examination Policy, to Technology Center Directors and Patent Examining Corps (Sept. 2, 2008), *available at* http://www.uspto.gov/web/patents/memoranda.htm.

[4] *Id.* at 1.

[5] *Id.* at 2.

[6] No. 2007-3300, 2008 WL 5105055 (Bd. Pat.App. & Inter., Nov. 19, 2008).

post-issuance patent infringement cases held "that the definiteness requirement 'does not compel absolute clarity' and '[o]nly claims "not amenable to construction" or "insolubly ambiguous" are indefinite.'"[7] Recognizing that this court has never set forth a different standard of review for indefiniteness under 35 U.S.C. § 112, second paragraph, for pre-issuance pending claims as compared with post-issuance patent claims,[8] the Board concluded that the Federal Circuit's reading of the indefiniteness requirement was counter to the PTO's broader standard for claim construction during prosecution.[9] Accordingly, the Board announced that, "rather than requiring that the claims are insolubly ambiguous, we hold that if a claim is amenable to two or more plausible claim constructions, the USPTO is justified in requiring the applicant to more precisely define the metes and bounds of the claimed invention by holding the claim unpatentable under 35 U.S.C. § 112, second paragraph, as indefinite."[10]

The Board is clearly right in recognizing that the circumstances are different between pre-issuance and post-issuance application of the definiteness standard with regard to claim terms. At the same time, the PTO and the Board are clearly right in insisting that, if the public notice function of the patent law is to be honored, claim terms must particularly point out and distinctly claim the subject matter of the invention. In my view, this court's definiteness doctrine could go considerably further in promoting that objective than

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[7] *Id.* at *4 (quoting *Datamize*, 417 F.3d at 1347).

[8] *Id.* at *6.

[9] *Id.* at *5.

[10] *Id.*

it currently does, with the not inconsequential benefit of shifting the focus from litigation over claim construction to clarity in claim drafting.

To begin the discussion of how this court could move in that direction, I would grant the petition for panel rehearing. The court now spends a substantial amount of judicial resources trying to make sense of unclear, overbroad, and sometimes incoherent claim terms. It is time for us to move beyond sticking our fingers in the neverending leaks in the dike that supposedly defines and figuratively surrounds a claimed invention. Instead, we might spend some time figuring out how to support the PTO in requiring that the walls surrounding the claimed invention be made of something other than quicksand.

I respectfully dissent from the loss of that opportunity through the panel's denial of rehearing.

APPENDIX D

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF CONNECTICUT

[Filed Aug. 18, 2005]

No. 3:04-CV-929 (JBA)

ENZO BIOCHEM, INC., ENZO LIFE SCIENCES, INC., and YALE UNIVERSITY,
Plaintiffs,

v.

APPLERA CORPORATION and TROPIX, INC.,
Defendants.

EXPERT REPORT OF LARRY J. KRICKA, D.Phil

* * * *

21. The ability of two complementary nucleic acid strands to hybridize can be used to perform a variety of tests. For instance, in hybridization assays, described in more detail in Section IV.D., a scientist will select or synthesize a nucleic acid with a known sequence of nucleotides, called a *probe*, specifically because the probe will hybridize with a complementary sequence of nucleotides in a target nucleic acid. This target nucleic acid, called an *analyte* or *target*, is usually a nucleic acid in a biological sample that the scientist wishes to detect the existence of, and possibly measure the amount of, in the sample. The probe will bind strongly and preferentially to complementary sequences in the analyte under hybridizable conditions creating a hybrid. After separating unhybridized probes or analyte from the hybrids by washing, the hybrids can be detected through use of a

label attached to or incorporated into the probe or the analyte. A label is a compound or an atom that has properties that make it either directly or indirectly detectable. (*See* Section IV.B. below on direct and indirect labeling.) Figure 6, shows an example of a basic hybridization assay where (1) nucleic acids from a sample are immobilized on a surface, (2) labelled probe is added, (3) unhybridized probe is washed away, and (4) the hybrids of labelled probe and analyte are detected by detecting the probe's label.

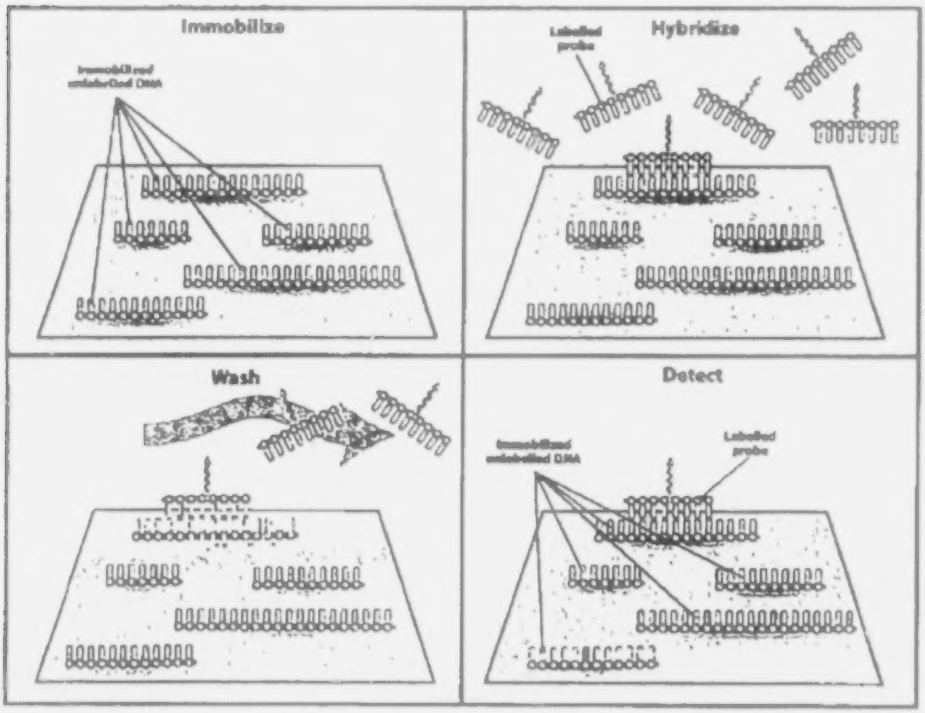


Figure 6

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